MAR 6 1961

MARCH 1961
VOL. 3 NO. 3

Journal of Occupational Medicine

IN THIS ISSUE

ORIGINAL ARTICLES:

- THE EDWIN SMITH PAPYRUS: EARLY EXPERIENCES IN INDUSTRIAL SURGERY?—THE 1960 RAMAZZINI ORATION ..... *Lemuel C. McGee, M.D.*
- DETERMINANTS OF ISCHEMIC ELECTROCARDIOGRAPHIC ABNORMALITIES AND CHEST PAIN—PART II. THE EXERCISE ELECTROCARDIOGRAM TEST ..... *Richard Gubner, M.D.*
- PHYSICAL FITNESS AND MOTOR VEHICLE ACCIDENTS ..... *Robert P. Sim, M.D., and Harold Brandaleone, M.D.*

SURGICAL REVIEW:

- THE TREATMENT OF INDUSTRIAL HAND INJURIES—PART III. BONE AND JOINT INJURIES ..... *Burton C. Kilbourne, M.D., and Eudell G. Paul, M.D.*

CASE REPORTS:

- ORGANIC PHOSPHATE INSECTICIDE POISONING ..... *David H. Reeder, M.D.*

SPECIAL SUPPLEMENT

ACUTE RADIATION DEATH RESULTING FROM AN ACCIDENTAL NUCLEAR CRITICAL EXCURSION

From the Los Alamos Scientific Laboratory, University of California, Los Alamos, N. M.

OFFICIAL PUBLICATION OF THE INDUSTRIAL MEDICAL ASSOCIATION

preferred for the treatment table because

Neo-Polycin Ointment

helps clear topical infections promptly

Neo-Polycin® provides neomycin, bacitracin and polymyxin, the three antibiotics preferred for topical use because these agents are rarely used systemically. This combination is effective against the *entire* range of bacteria causing most topical infections... has a low index of sensitivity... and does not interfere with wound healing. And Neo-Polycin provides these three antibiotics in the unique Fuzene® base, which releases a higher concentration of antibiotics than is possible with grease-base ointments.

Each gram of Neo-Polycin contains 3 mg. of neomycin, 400 units of zinc bacitracin and 8000 units of polymyxin B sulfate in the unique Fuzene base. Supplied in 15 Gm. tubes.

PM PITMAN-MOORE COMPANY
DIVISION OF ALLIED LABORATORIES, INC., INDIANAPOLIS 8, INDIANA

Vol. 3 No. 3

Journal of Occupational Medicine

ISSUE OF MARCH 1961

Official Publication of the Industrial Medical Association

TABLE OF CONTENTS

TEXT SECTION

Original Articles

THE EDWIN SMITH PAPYRUS: EARLY EXPERIENCES IN INDUSTRIAL SURGERY? THE 1960 RAMAZZINI ORATION 101
Lemuel C. McGee, M.D., Wilmington, Del.

DETERMINANTS OF ISCHEMIC ELECTROCARDIOGRAPHIC ABNORMALITIES AND CHEST PAIN—PART II. THE EXERCISE ELECTROCARDIOGRAM TEST 110
Richard Gubner, M.D., New York, N.Y.

PHYSICAL FITNESS AND MOTOR VEHICLE ACCIDENTS 121
Robert P. Sim, M.D., and Harold Brandaleone, M.D., New York, N.Y.

Surgical Review

THE TREATMENT OF INDUSTRIAL HAND INJURIES—PART III. BONE AND JOINT INJURIES 123
Burton C. Kilbourne, M.D., and Eudell G. Paul, M.D., Chicago, Ill.

Case Reports

ORGANIC PHOSPHATE INSECTICIDE POISONING 129
David H. Reeder, M.D., Whittier, Calif.

President's Message 131

Book Reviews 132

Publications Available 133

Questions 134

Abstracts of Current Literature

CLINICAL TOXICOLOGY 135
INDUSTRIAL HYGIENE CONTROLS 136
MEDICAL CARE ADMINISTRATION 137
DERMATOLOGY 138
EXPERIMENTAL TOXICOLOGY 139
SURGERY 140
NOISE AND HEARING 141

Abstracts—Continued

RADIATION 142
INTERNAL MEDICINE 143

SPECIAL SUPPLEMENT

ACUTE RADIATION DEATH RESULTING FROM AN ACCIDENTAL NUCLEAR CRITICAL EXCURSION 145
Thomas L. Shipman, M.D., C. C. Lushbaugh, M.D., Donald F. Petersen, Ph.D., Wright H. Langham, Ph.D., Payne S. Harris, M.D., and James N. P. Lawrence, M.A., Los Alamos, N.M.

GENERAL SECTION

Industrial Medical Association

NOMINEES FOR OFFICERS AND DIRECTORS *8a*

PROPOSED CHANGES IN BY-LAWS *12a*

PROGRAM, TOXICOLOGY AND INDUSTRIAL HYGIENE SESSIONS *13a*

ANNUAL BANQUET *14a*

About the Authors *17a*

Directory of Advertisers *18a*

People and Events *19a*

IN COMING ISSUES

APPLICATION OF WORKMEN'S COMPENSATION LAWS TO RADIATION INJURIES
John K. Dane, Boston, Mass.

THE FUNCTIONS AND AIMS OF THE UNITED WIRE, METAL AND MACHINE MEDICAL CENTER
Bernard Rothbard, M.D., New York, N.Y.

PSYCHIATRY IN INDUSTRY AS SEEN BY AN INDUSTRIAL PHYSICIAN
E. F. Buyniski, M.D., Cincinnati, Ohio

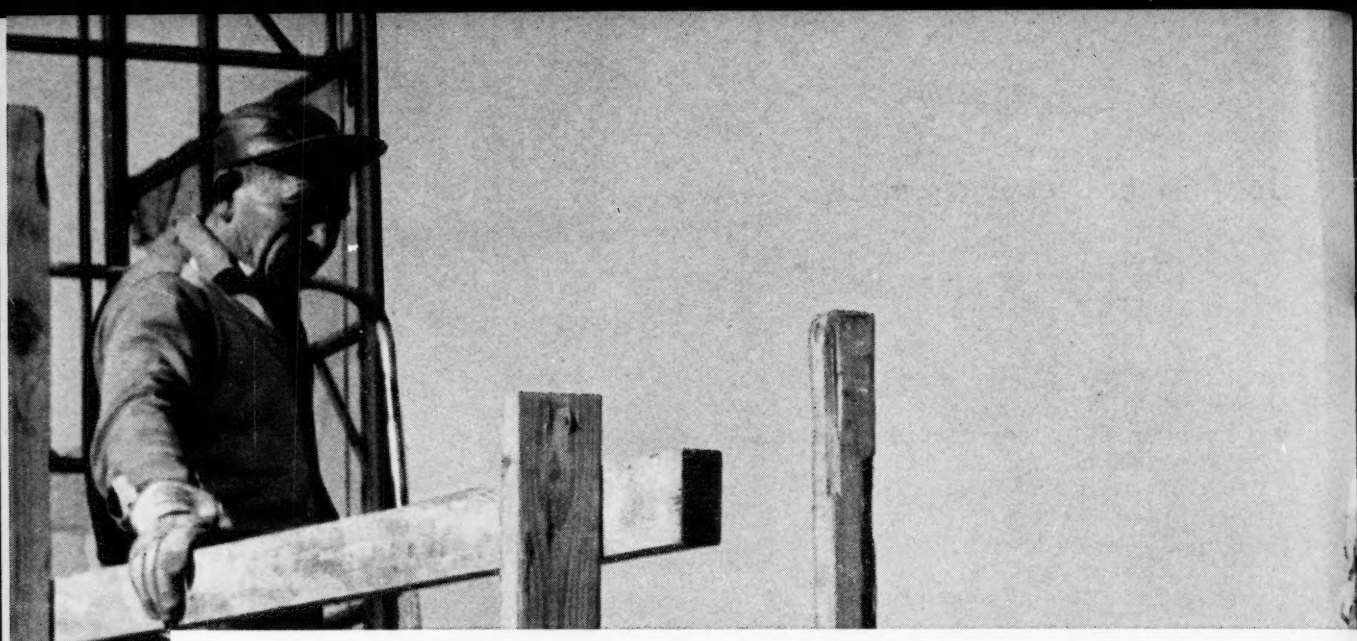
Journal of Occupational Medicine is published by the Industrial Medical Association, 28 East Jackson Boulevard, Chicago 4, on the 1st of each month. Second class postage paid at Chicago, Illinois. Copyright 1961 by the Industrial Medical Association. Title registered, United States Patent Office.

Subscriptions $10.00 per year; $25.00 for three years—U. S. and foreign. Single copies $1.00 postpaid. Make checks payable to Journal of Occupational Medicine.

Subscriptions, changes of address, and all business matters should be addressed to Clark D. Bridges, Publication Manager, Journal of Occupational Medicine, 28 East Jackson Boulevard, Chicago 4, Ill.

Manuscripts submitted for publication should be sent direct to the Editor, Adolph G. Kammer, M.D., 2057 Beechwood Boulevard, Pittsburgh 17, Pa.

Change of address notices received by the 15th of any month will assure delivery of the following month's issue. Address change is facilitated if old address is also furnished.



Put your low-back patient back on the payroll

Soma's prompt relief of pain and stiffness can get your low-back patients back to work in days instead of weeks

Soma is unique because it combines the properties of an effective muscle relaxant and an independent analgesic in *a single drug.* Unlike most other muscle relaxants, which can only relax muscle tension, Soma attacks both phases of the pain-spasm cycle at the same time.

Thus with Soma, you can break up both pain and spasm fast, effectively . . . help give your patient the two things he wants most: relief from pain and rapid return to full activity.

Soma is notably safe. Side effects are rare. Drowsiness may occur, but usually only with higher dosages. Soma is available in 350 mg. tablets. USUAL DOSAGE: 1 TABLET Q.I.D.

The muscle relaxant with an independent pain-relieving action

SOMA®

(carisoprodol, Wallace)

Wallace Laboratories, Cranbury, New Jersey

How you can help save your patients a month's pay

Kestler reports in J.A.M.A. (April 30, 1960) that conventionally treated low-back syndrome patients required an average of 41 days for full recovery (range: 3 to 90 days). The addition of Soma therapy in this comparative investigation reduced the average to 11.5 days (range: 2 to 21 days). With Soma, patients averaged full recovery 30 days sooner.

Journal of Occupational Medicine

Official Publication of the Industrial Medical Association

Editor:

ADOLPH G. KAMMER, M.D.
University of Pittsburgh
Pittsburgh, Pa.

Assistant Editors:

EDWARD V. HENSON, M.D.
Chicago, Ill.

CHARLES E. LEWIS, M.D., Sc.D.
Kansas City, Kansas

Editorial Board:

PAUL J. BAMBERGER, M.D.
Bethlehem, Pa.

RUSSELL G. BIRRELL, M.D.
Toronto, Ont.

RONALD F. BUCHAN, M.D.
Boston, Mass.

ROBERT C. COMBS, M.D.
San Francisco, Calif.

FRANK PRINCI, M.D.
Cincinnati, Ohio

IRWIN SCHULZ, M.D.
Milwaukee, Wis.

Publication and Business Office

28 East Jackson Blvd.
Chicago 4, Ill.

Publication Manager:

CLARK D. BRIDGES

Assistant Publication Manager:

DORIS L. FLOURNOY

LITERATURE ABSTRACTERS

Dermatology

RAYMOND R. SUSKIND, M.D.
Cincinnati, Ohio

DONALD J. BIRMINGHAM, M.D.
Cincinnati, Ohio

WILLIAM R. BUCKLEY, M.D.
Rochester, N. Y.

MARCUS M. KEY, M.D.
Cincinnati, Ohio

LEO J. MIEDLER, M.D.
Ann Arbor, Mich.

Noise & Hearing

H. O. PARRACK, Ph.D.
Wright-Patterson AFB, Ohio

RONALD G. HANSEN, Ph.D.
Enon, Ohio

W. DIXON WARD, Ph.D.
Los Angeles, Calif.

Environmental Physiology

DAVID MINARD, CAPT., MC, USN
Bethesda, Md.

HARRY J. ALVIS, CAPT., MC, USN
United States Pacific Fleet

ROBERT T. CLARK, Ph.D.
Oklahoma City, Okla.

Experimental Toxicology

ROBERT E. ECKARDT, Ph.D., M.D.
Linden, N. J.

Industrial Hygiene Controls

EDWARD C. RILEY, M.D.
Rochester, N. Y.

MORRIS KLEINFELD, M.D.
New York, N. Y.

LOUIS W. SPOLYAR, M.D.
Indianapolis, Ind.

Internal Medicine

JOHN J. THORPE, M.D.
New York, N. Y.

LEO J. WADE, M.D.
New York, N. Y.

SHERMER H. STRADLEY, JR., M.D.
Wilmington, Del.

Medical Care Administration

ASA BARNES, M.D.
Louisville, Ky.

JOHN D. WINEBRENNER, M.D.
Knoxville, Tenn.

Mental Health

GRAHAM C. TAYLOR, M.D.
Montreal, Que.

KENNETH J. MUNDEN, M.D.
Topeka, Kans.

ALAN McLEAN, M.D.
New York, N. Y.

Clinical Toxicology

LEE H. MILLER, M.D., I.M.D.
Cincinnati, Ohio

ALVIN DAVIS, M.D.
Cincinnati, Ohio

M. C. BATTIGELLI, M.D.
Pittsburgh, Pa.

OTTO P. G. PREUSS, M.D.
Columbus, Ohio

Radiation Health

THOMAS S. ELY, M.D.
Washington, D. C.

W. DAGGETT NORWOOD, M.D.
Richland, Wash.

GEORGE L. VOELZ, M.D.
Idaho Falls, Idaho

Surgery

ROBERT J. TRETTIN, M.D.
Milwaukee, Wis.

JOSEPH T. ANDREWS, M.D.
Buffalo, N. Y.

NORMAN B. HODGSON, M.D.
Milwaukee, Wis.

DERWARD LEPLEY, JR., M.D.
Milwaukee, Wis.

OWEN E. MILLER, M.D.
Milwaukee, Wis.

PAUL NATVIG, M.D.
Milwaukee, Wis.

SANFORD SIMON, M.D.
Kansas City, Mo.

SUGGESTIONS TO AUTHORS

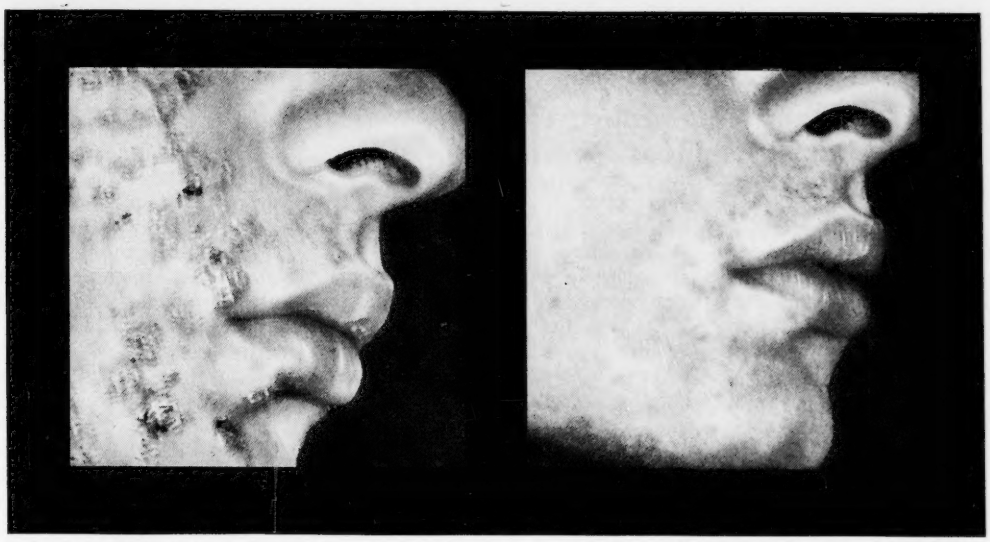
Materials for publication should be addressed to the Editor, 2057 Beechwood Blvd., Pittsburgh 17. Articles will be considered for publication on condition that they are submitted solely to *Journal of Occupational Medicine*.

The manuscript, including references, footnotes, and legends for illustrations, should be typed on one side of a standard-sized page of opaque paper, double-spaced, and with at least a one inch margin at each edge. One carbon copy should accompany the original typescript, and the author should retain a carbon copy for use in reading proofs.

The authors' names should be accompanied by the highest academic or medical degrees that they hold; letters indicating membership in honor or professional societies will not be published. Authors who are in the armed services should not use civilian degrees in connection with their names. The city of each author should be supplied, and an address should be provided at the end of the manuscript for the use of readers who may wish to communicate with the senior author. If academic, hospital, or industrial connections are given for one author, they must be given for all other authors who have such connections. The authors are responsible for obtaining permission from the proper authorities to use the names of institutions.

References to the literature should be limited to those used in preparation of the manuscript; they should be typed on a special page at the end of the manuscript and should be in the style of those used in the scientific publications of the American Medical Association. Titles of all articles must be given.

Charts and drawings should be in black ink on hard, white paper. Lettering should be large enough to permit necessary reduction. Oversized illustrations should be photographed and a glossy print submitted. Prints of a bluish tinge will not reproduce well. Paper clips must not be used on prints, since the marks left will show in the reproduction. A label should be pasted to the back of each illustration showing its number, the author's name, an abbreviated title of the article, and an indication of the top of the picture. Each chart and illustration must have a descriptive legend, and each table must have a caption.



Infectious folliculitis with secondary impetiginization treated with FURACIN-HC Cream—*6 days later improved and discharged.*

Pyodermas: fight infection, facilitate healing

In clinical use for more than 13 years and today the most widely prescribed single topical antibacterial, FURACIN *retains undiminished potency against pathogens such as staphylococci that no longer respond adequately to other antimicrobials.* FURACIN *is gentle, nontoxic to regenerating tissue, speeds healing through efficient prophylaxis or prompt control of infection. Unique water-soluble bases provide thorough penetration, lasting activity in wound exudates, without "sealing" the lesion or macerating surrounding tissue.*

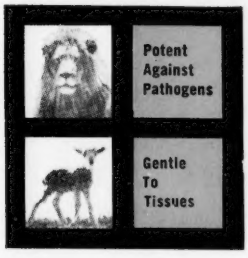
Eaton®

the broad-spectrum bactericide exclusively for topical use

FURACIN®

brand of nitrofurazone

in dosage forms for every topical need



Soluble Dressing / Soluble Powder
Solution / Cream / HC Cream
(with hydrocortisone) / Vaginal
Suppositories / Inserts / FURESTROL®
Suppositories (with diethylstilbestrol)
Special Formulations for Eye, Ear, Nose

EATON LABORATORIES
Division of The Norwich Pharmacal Company
NORWICH, NEW YORK

Association Activities

Officers and Directors Nominated; Election To Be Held at Annual Business Meeting

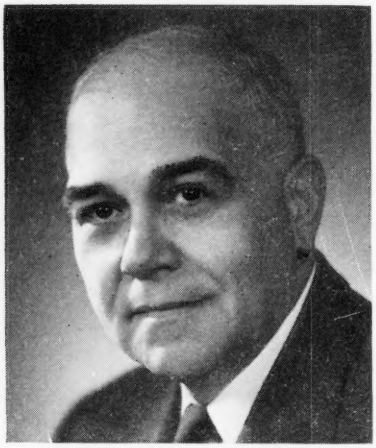
GRADIE R. ROWNTREE, M.D., President-Elect of the Industrial Medical Association will be installed as President at the conclusion of the Association's annual meeting in Los Angeles, April 11-13. Nominations for the other offices have been made by the Board of Directors advancing the First and Second Vice-Presidents in the line of succession to the presidency. Thus, H. GLENN GARDINER, M.D., has been nominated for President-Elect, and JOHN L. NORRIS, M.D., has been nominated for First Vice-President. JERMYN F. MCCAHAN, M.D., has been nominated to succeed himself as Treasurer. The two new nominees for offices of the Association are EDWARD J. SCHOWALTER, M.D., who has been nominated for Second Vice-President, and EMMETT B. LAMB, M.D., who has been nominated for the office of Secretary.

Candidates for the Board of Directors are nominated by the Nominating Committee with the approval of the Board of Directors. Ten members have been nominated for the term 1961-1964. Five are to be elected. Names of all nominees will appear on the prepared ballot which will be distributed at the annual business meeting April 12 in Los Angeles. Further nominations, however, may be made from the floor, and names may be written in on the ballot.

Brief biographical information about the nominees for Second Vice-President and Secretary and about each candidate for directorship follows:

EDWARD J. SCHOWALTER—General Medical Director, Western Electric Company, Inc., New York City; M.D. degree from Loyola University Medical School (now called the Stritch School of Medicine of Loyola), 1936; certified by the American Board of Preventive

President-Elect and Nominees for Other Offices



Gradie R. Rowntree, M.D.
President-Elect

H. Glenn Gardiner, M.D.
Nominee for President-Elect

John L. Norris, M.D.
Nominee for First Vice-President

Edward J. Schowalter, M.D.
Nominee for Second Vice-President

Emmett B. Lamb, M.D.
Nominee for Secretary

Jermyn F. McCahan, M.D.
Nominee for Treasurer

Association Activities

Medicine in Occupational Medicine, 1955; Fellow, American Academy of Occupational Medicine; Fellow, American Academy of Preventive Medicine. IMA activities: member, 1942; Fellow, 1952; Director, 1954-1956; past chairman, Workmen's Compensation Committee; present chairman, Ad Hoc Committee on Organization; past President, Central States Society of Industrial Medicine and Surgery, 1957-1958.

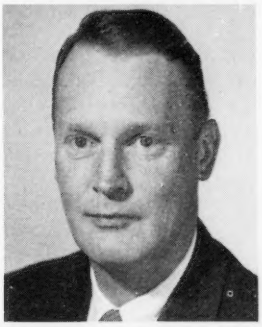
EMMETT B. LAMB—Physician-in-Charge, Indianapolis Works, International Harvester Company; Medical Director, P. R. Mallory, Inc.; lecturer in industrial medicine, Indiana University School of Medicine; M.D. degree from Indiana University School of Medicine, 1931; Fellow, American College of Surgeons; Fellow, International College of Surgeons; Chairman, Commission of Public Health of the Indiana State Medical Association. IMA activities: member, 1942; Fellow, 1947; Director, 1958-1961; past District Counselor for Indiana.

ASA BARNES—Area Medical Administrator, United Mine Workers Association Welfare and Retirement Fund, Louisville, Ky.; Associate Professor of Community Health and Acting Chairman, Department of Physical Medicine and Rehabilitation, University of Louisville School of Medicine; Assistant Clinical Professor of Industrial Medicine, Department of Preventive Medicine and Industrial Health, College of Medicine, University of Cincinnati; M.D. degree from University of Tennessee, 1931; M.P.H. degree from Johns

Nominees for the Board of Directors, 1961-1964

(Five to be Elected)

Asa Barnes, M.D.



Preston N. Barton, M.D.

Lewis C. Benesh, M.D.

James Frenkil, M.D.

David D. Holaday, M.D.

Eugene P. Owen, M.D.

John F. Shronts, M.D.

Gordon A. Sinclair, M.D.

Richard A. Sutter, M.D.

Robert A. Wise, M.D.

Association Activities

Hopkins University, 1940; Fellow, American Public Health Association, 1940; Diplomate, American Board of Preventive Medicine, 1950; Fellow, American College of Preventive Medicine, 1951; member, Association of Teachers of Preventive Medicine; member, Association of Military Surgeons; Colonel, M.C., USAR and C.O. 306 General Hospital, USAR; member, Group Health Association of America; IMA activities: member, 1952; Fellow, 1957; member, Committee on Medical Care, 1954-1957, chairman of the committee, 1957 to present; member, Executive Committee, Kentucky Industrial Medical Association, 1958-1960; Abstractor, Medical Care Administration, JOURNAL OF OCCUPATIONAL MEDICINE 1959 to present.

PRESTON N. BARTON—Medical Director, New Departure Division of General Motors Corporation, Meriden, Conn.; M.D. degree from Harvard Medical School, 1939; Fellow, American College of Preventive Medicine; Fellow, American Academy of Occupational Medicine; Board of Directors, Connecticut Academy of Preventive Medicine, 1960 to present; member, State Committee on Industrial Health, Connecticut State Medical Society 1948 to present, chairman, 1952-1955; member, Committee on Occupational Health and Safety, Connecticut State Manufacturers Association, 1953 to present; Diplomate, American Board of Preventive Medicine, certified in Occupational Medicine, 1955; member of the Committee to develop "Guiding Principles for the Physician in Industry" of the Council on Industrial Health, American Medical Association, 1953-1954. IMA activities: member, 1947; Fellow, 1952; member, Committee on Practice 1954-1958, chairman, 1958; member, Committee on Medical Care and Practice 1958-1959, Chairman on Industrial Medical Practice 1959 to present; President, New England Industrial Medical Association, 1955-1956.

L. C. BENESH—Regional Medical Director for United Air Lines, Denver, Colo.; M.D. degree from Rush Medical College of the University of Chicago, 1928; member, Airline Medical Directors Association and Aerospace Medical Association; chairman, Industrial Health Committee, Colorado State Medical Society, 1958 to present and chairman of the Joint Conference of State Chairmen to be held in Denver in October, 1961. IMA activities: member, 1947; Fellow, 1959; President, Rocky Mountain Academy of Industrial Medicine; District Counselor, 1959 to present.

JAMES FRENKIL—Director, Central Medical Centre, Baltimore, Md.; Chief, Industrial Medical and Occupational Disease Department of North Charles General Hospital, Baltimore; M.D. degree from University of Maryland, 1937; Captain, U. S. Army Air Corps, 1943-1946; School of Aviation Medicine, 1945; member, Aviation Medical Association; American Medical Writers Association; Medical and Chirurgical Faculty of Maryland; Fellow, American Academy of Occupational Medicine; contributing editor in industrial medicine to *Current Medical Digest;* chairman, Board of Occupational Diseases of the State of Maryland, 1953 to present; Secretary, Section on Industrial Medicine and Surgery, Southern Medical Association, 1960, and Vice-Chairman, 1961. IMA activities; member, 1948; Fellow, 1952.

DAVID D. HOLADAY—Western Area Physician, American Can Company, San Francisco, Calif.; Assistant Clinical Professor, Occupational Medicine, Stanford University; M.D. degree from University of Kansas, 1935; M.P.H. degree, University of California, 1948; Diplomate, American Board of Preventive Medicine, certified in Occupational Medicine, 1955. IMA activities: member, 1950; Fellow, 1956; member, Membership Committee, 1959 to present; President, Western Industrial Medical Association, 1957-1958.

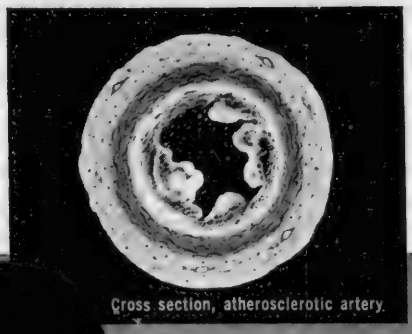
EUGENE P. OWEN—Internist, private practice, Portland, Ore.; Medical Director, Western Area Consolidated Freightways, Freightliner Corporation, West Coast Steamship Company, and the Federal Reserve Bank, Portland Branch; Medical Consultant, Standard Oil of California and the Carnation Company; M.D. degree from Harvard School of Medicine, 1929; Captain, MC USNR, retired; past President, Oregon Academy of Occupational Medicine; past President, Northwest Association of Occupational Physicians; licensed examiner, Civil Aeronautics Board Commercial Pilots. IMA activities: member, 1955; Fellow, 1959; member, Committee on Standards for Motor Vehicle Driving.

JOHN F. SHRONTS—Medical Director, General Mills, Inc., Minneapolis, Minn.; M.D. degree from Northwestern University Medical School, 1936; Diplomate and founder, American Board of Preventive Medicine, certified in Occupational Medicine, 1955; member, American Public Health Association. IMA activities: member, 1946; Fellow, 1952; Director, 1955-1957; District Counselor, 1954-1955, 1958 to present; Public Relations Committee, 1952-1953; Membership Committee, 1947-1948, Committee on Problem Drinking, 1957-1961; Central States Society of Industrial Medicine and Surgery, Board of Governors, 1948-1950, program co-chairman, 1953-1954; President, Minnesota Academy of Occupational Medicine and Surgery, 1955, and member, Executive Committee, 1956-1961.

GORDON A. SINCLAIR—Assistant Medical Director, Imperial Oil, Ltd., Toronto, Ontario; M.D., degree from University of Toronto, 1926; chairman, Industrial Section, Ontario Medical Association, 1952-1953; chairman, Section on Industrial Medicine, Academy of Medicine, 1949-1950; Fellow, American Academy of Occupational Medicine; Diplomate, American Board of Preventive Medicine, certified in Occupational Medicine, 1955; Certified Specialist in Internal Medicine, Royal College of Physicians and Surgeons (Canada). IMA activities: member, 1947; Fellow, 1954.

RICHARD A. SUTTER—Director Sutter Industrial Clinic, St. Louis, Missouri; M.D. degree from Washington University (St. Louis), 1935; Fellow, American College of Preventive Medicine and the American Medical Association; member, American Association of Railway Surgeons and the American Public Health Association; Diplomate, American Board of Preventive

outstanding nutritional research achievement



Cross section, atherosclerotic artery.

to aid in the dietary control of serum cholesterol

MAZOLA®

U.S. Pat. No. 2,955,039

MARGARINE
scientifically formulated with pure liquid **non-hydrogenated** MAZOLA Corn Oil.

MAZOLA Margarine is an economical tablespread and serves as a solid shortening, rich in linoleates and low in saturates—making it an ideal dietary adjunct in the management of serum cholesterol. It contains 2 to 3 times as much natural linoleic acid as any other margarine readily available in grocery stores from coast to coast, and 5 to 8 times as much as butter. It contains no dairy or animal fats, no coconut oil, and no cholesterol.

MAZOLA Margarine is indistinguishable from other quality margarines as to taste, aroma and handling characteristics. Thus, it can be part of the regular diet for the whole family, including the hypercholesterolemic patient. The major ingredient in MAZOLA Margarine—liquid MAZOLA Corn Oil—is NOT hydrogenated, thereby preserving its rich content of linoleates.

The average daily intake, two ounces or 56.8 Gm. (4 tablespoons) of MAZOLA Margarine, supplies

Linoleic acid	12 Gm.
Oleic acid	23 Gm.
Saturated fatty acids	8 Gm.
Plant sterols (sitosterols)	215 mg.
Natural tocopherols	30 mg.
Vitamin A	1870 USP units
Vitamin D	250 USP units
Calories	415

Available in the refrigerator sections of grocery stores in the same general price range as other premium quality margarines, in 1-lb. packages (four ¼ lb. sticks).

Send for free booklet:
"Recent Advances in the Dietary Control of Hypercholesterolemia."

BEST FOODS • Division of Corn Products Co., NEW YORK 22, N. Y.

Association Activities

(Continued from page 10a)

Medicine, certified in Occupational Medicine, 1956. IMA activities: member, 1946; Fellow, 1953; District Counselor, 1951-1952; Deputy General Chairman, Industrial Health Conference, 1957; member, Committee on Surgery of Trauma, 1953-1955; member, Health Achievement in Industry Award Committee, 1956-1958, chairman, 1958 to present; Board of Governors, Central States Society of Industrial Medicine and Surgery, 1952-1955, 1961-1963, and President, 1959-1960.

ROBERT A. WISE—Assistant Chief Physician, Humble Oil & Refining Company, Houston, Tex.; M.D. degree from Washington University, St. Louis, 1936; IMA activities: member, 1953; Fellow, 1957; District Counselor, 1955 to present; President-Elect, Texas IMA; President, Houston Society Internal Medicine; Fellow, American College of Physicians; American Board of Internal Medicine.

Recommended Changes in IMA By-Laws To Be Voted Upon at Annual Business Meeting

The By-Laws Committee and the Board of Directors of the Industrial Medical Association have approved and recommend the following changes to the By-Laws. These will be presented to the membership for action at the Annual Business Meeting in Los Angeles on April 12, 1961. For reference, the current By-Laws were published in full in the September, 1959, issue of the JOURNAL OF OCCUPATIONAL MEDICINE, pp. *16a-19a*. A copy of the complete By-Laws and of the proposed changes will be given each member attending the Annual Business Meeting.

Article VI—Meetings of Members

SECTION 5—Delete last sentence "Exception to the above . . ."

Article VII—Meetings of the Board of Directors

SECTION 1, second sentence—Change to read: "Special meetings of the Board of Directors may be called by the President or by any five (5) Directors at such time and place as shall be designated in the call."

SECTION 2—Add: Quorum: "A majority of the Board of Directors shall constitute a quorum."

Article VIII—Election of Officers and Directors

SECTION 3—Delete.

SECTION 4—Renumber as Section 3.

SECTION 5—Renumber as Section 4 and change to read: "The Nominating Committee shall furnish the Board of Directors their nominations at least three (3) months prior to the next Annual Meeting of the Members. The Managing Director shall have ballots printed with the nominations as recommended by the Board of Directors and space will be allowed on the ballot for write-in votes for each office. The candidates receiving the greatest number of votes shall be elected.

Vitamins are
PART OF THE PICTURE
"WE REALIZE that our in-plant medical care and safety measures cannot be fully effective if outside environment and habits rob our employees of alertness and ability to perform efficiently.
"That's why our bulletin boards stress safe driving, regular physical examinations, and principles of good nutrition.
"Because we know our advice is not always followed, particularly on nutrition, we encourage our employees to avail themselves of vitamin supplements at low cost through the plant."
TO LEARN HOW VITAMINS FOR INDUSTRY CAN PROVIDE SUCH A PROGRAM FOR YOUR PLANT, VISIT US AT BOOTH 21, AMERICAN INDUSTRIAL HEALTH CONFERENCE, BILTMORE HOTEL, LOS ANGELES, APRIL 11, 12 AND 13, OR WRITE TO
Vitamins FOR INDUSTRY, INC.
3456 WEST OLYMPIC BOULEVARD
LOS ANGELES 19, CALIFORNIA

SECTION 6—Renumber as Section 5.

SECTION 7—Renumber as Section 6 and change to read: "Ballots shall be mailed by the Managing Director to those Members and Fellows eligible to vote by virtue of a paid-up membership, not later than eight (8) weeks prior to the Annual Meeting. These ballots must be returned to the Managing Director's office not later than four (4) weeks prior to the time of the Annual Business Meeting in order to be counted."

SECTION 8—Renumber as Section 7 and change to read: "The President shall not cast a ballot except in case of a tie vote. The results shall be announced before the close of the Annual Meeting."

SECTION 9—Renumber as Section 8 and change to read: "The mail ballot shall provide for the election to the Board of Directors, five (5) Fellows to serve for a term of three (3) years, and other Fellows to serve as Directors to fill the unexpired terms when vacancies arise."

SECTION 10—Renumber as Section 9.

Article XI—Dues

SECTION 1—Change to read: "The annual dues of Active Members shall be Thirty Dollars ($30.00) per year; of Fellows, Thirty-five Dollars ($35.00) per year; and of Associate Members, Fifteen Dollars ($15.00) per year. Honorary Members and Emeritus Members shall pay no dues. Such part of the dues of Component Society Members may be allotted to the respective Component Societies as may be from time to time determined by the Board of Directors."

Article III—Membership

SECTION 7—RETIRED MEMBERSHIP—Change to read: "Emeritus Membership: Fellows and Active Members who have been members of this Association for ten (10) years or more, and who are Fellows or Active Members in good standing at the time of their retirement or are Inactive Members by virtue of disability, or have been Active Members for twenty (20) years or more and have reached the age of seventy (70), shall be eligible to Emeritus Membership. Each case must be acted upon and approved by the Executive Committee."

Association Activities

Program for Toxicology and Industrial Hygiene Sessions of IMA Meeting Announced

The program for the Toxicology and Industrial Hygiene sessions of the Industrial Medical Association's Forty-Sixth Annual Meeting in Los Angeles has just been completed. The all-day general session to be held April 13 has been arranged jointly by the Scientific Committee on Clinical Toxicology of the Industrial Medical Association and the Southern California Section of the American Industrial Hygiene Association.

The entire program will be devoted to a consideration of "Industrial Hygiene Problems in the Missile Industries." EDWARD K. DANIELS will preside at the morning session which includes the following presentations: "Communication in Industrial Hygiene"—MAJ. ROBERT T. P. DE TREVILLE, USAF, MC; "Control of Occupational Health Hazards in Aerospace and Missile Industries"—MEYER SCHNEIDER and TOBY FREEDMAN, M.D.; "Control of Industrial Hygiene Problems in a Missile Industry"—REX B. GORDON; "Review of Nitrogen Tetroxide Exposure in a Missile Industry"—PATRICK J. CLANCY, M.D.; "Experience with Unsymmetrical Dimethylhydrazine Exposure in a Missile Industry"—B. DWIGHT CULVER, M.D.; "Steel Plant Heat Stress in a Semi-Arid Region"—H. A. LEWIS, M.D., and ZEB G. BELL, JR.; "Borane Exposure in Industry"—GEORGE ROUSH, JR., M.D., and RUTHERFORD T. JOHNSTONE, M.D.; "Experiences with Symptoms and Solvents"—JOSEPH B. RUFFIN, M.D.; "Acute Pulmonary Disease Apparently Resulting from Exposure to Epoxy-Resin Coated Fiberglass Dust"—JOSEPH F. BOYLE, M.D., REGINALD H. SMART, M.D., and JACK C. ROGERS; "Pneumococciosis Case Finding in Industry—Review of a Technique Used in Four Plants"—CAPT. J. R. EASON, USAF, MC; "Occupational Health in the Aluminum Industry"—JAMES P. HUGHES, M.D., and PAUL R. EBLING, M.D.

MAJ. ROBERT T. P. DE TREVILLE will preside at the afternoon session which includes the following presentations: "Observations in Uranium Mining and Milling"—HAROLD J. MAGNUSON, M.D,. and VICTOR E. ARCHER, M.D.; "Air Force Experience with Microwave Exposure"—COL. JOHN E. BOYSEN, USAF, MC; "Potential Nuclear Hazards in U.S. Air Force Operations"—COL. ALVIN F. MEYER, USAF, MSC, and BRIG. GEN. THEODORE C. BEDWELL; "Effect of Radiation Upon Human Health and Life Span"—HARDIN B. JONES, M.D.; "Medical Records of Exposure to Known Toxic Agents"

MAdison 4-7581

is the number to telephone in Los Angeles to reach the special Message Center that will be in operation at The Biltmore Hotel during the scientific sessions of the Industrial Medical Association's annual meeting and the American Industrial Health Conference, April 11-13. Staffed by expert telephone personnel, this Message Center is a special convention service provided through the courtesy of The Pacific Telephone & Telegraph Company.

The Message Center will handle incoming calls (and written messages) for Conference participants and will post the names of persons for whom they have messages. The Hospitality Committee will endeavor to locate individuals for whom there are emergency calls.

MAdison 4-7581 is a direct wire to the Message Center. In addition, the switchboard of The Biltmore will also have a connection into the Message Center. The phone number of The Biltmore is MAdison 4-1011.

The Message Center will be located adjacent to the exhibit area and will be in operation from 9:00 a.m. to 5:15 p.m. on Tuesday and Wednesday, and from 9:00 a.m. to 3:30 p.m. on Thursday. Attendants will also provide change for nearby coin telephones for return messages.

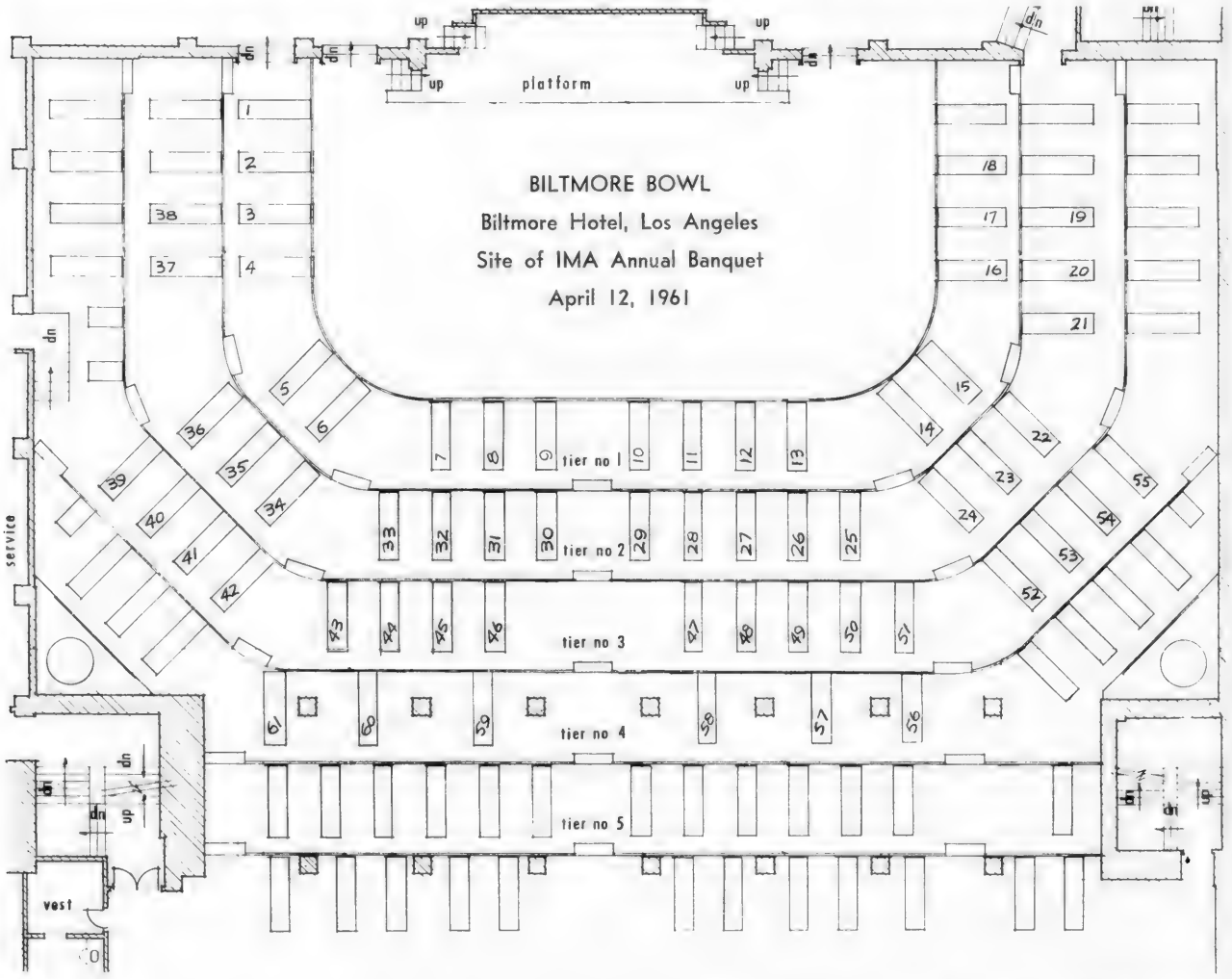
—CAPT. ROBERT T. MAYKOSKI, USAF, MSC, MAJ. DE TREVILLE, WARREN L. SMITH, M.D., and CAPT. EDWARD STOECKLE, USAF, MSC; "Toxicity Problems Encountered in the U.S. Air Force"—LIEUT. COL. LEE B. GRANT, USAF, MC; "Toxicity Problems Encountered in the U.S. Army"—LIEUT. COL. NORBERT E. ROSENWINKEL, USN, MC; "Industrial Hygiene Support to Rocket Test Operations"—CAPT. OWEN K. KITTILSTAD, USAF, MSC, LIEUT. COL. JOHN A. PETERSON, USAF, MC, and MAJ. HARRY R. BRATT, USAF, MC; "Operational Missile Medical Support"—CAPT. HAROLD W. DIETZ, USAF, MC, and LIEUT. JOHN J. MCCAMBRIDGE, USAF, MSC; "Air Force Environmental Health Laboratory Support to the Missile Program" — MAJ. ROBERT PETERSON, USAF, MSC.

IMA BANQUET TO BE GALA AFFAIR

ROBERT E. ECKARDT, M.D., IMA President, has decreed that there shall be no speeches and no speakers' table at this year's Association banquet on Wednesday, April 12 in the Biltmore Bowl, Biltmore Hotel, Los Angeles. Plans have been completed for a thoroughly pleasant evening including dinner with music, dancing until midnight, and some entertainment. The Association awards usually presented at the annual banquet will be presented during the IMA business meeting earlier in the day.

During the evening retiring President ECKARDT will announce the names of the new IMA Directors elected during the business meeting and will also make brief introductions of the award winners and other notables before turning the gavel over to the new President, GRADIE R. ROWNTREE, M.D.

Banquet chairman, RICHARD CALL, M.D., announces that advance reservations for dinner tickets will be accepted until April 1. Each table will seat eight persons and the cost is $10.00 per ticket. Reservations specifying table desired (see layout of Biltmore Bowl on this page) should be sent to the Industrial Medical Association, 28 East Jackson Blvd., Chicago 4, accompanied by remittance. Places will be assigned in order of receipt of applications. Table 5, 6, 7, 8, 9, 10, 11, 12, 13, and 29 are not available as they have been assigned to IMA officers, directors, distinguished guests, and their wives.



Journal of Occupational Medicine

The 1960 Ramazzini Oration

The Edwin Smith Papyrus: Early Experiences in Industrial Surgery?

Lemuel C. McGee, M.D., Wilmington, Del.

WHILE a graduate student at the University of Chicago, I attended lectures in a special course on the physiology of the nervous system given by a stimulating teacher, then in his prime, the late Prof. Arno B. Luckhardt. One afternoon at the designated lecture hour, Luckhardt entered the classroom with sleepy eyes and yet with an air of pent-up enthusiasm. In an attitude of sharing with his students a dramatic discovery, immediately he launched into a report of his activities of the previous night. He had been invited to the home of the distinguished Egyptologist, James Henry Breasted, to examine some notes regarding an extraordinary record of surgical practice in ancient Egypt and to promise assistance in selecting the proper medical and anatomic terms for the translation of the papyrus.

Luckhardt's lecture that day made no reference to experimental physiology of the central nervous system. The professor was enthralled by what he had seen and heard the previous night. This constituted my introduction to the Edwin Smith Surgical Papyrus.

As to Papyri in General

The word papyrus comes from *Cyperus papyrus,* the name of a plant which in ancient times was cultivated in the delta of Egypt (Fig. 1). It is now extinct in Lower Egypt but is still found in the Upper Nile regions and in Abyssinia.

Theophrastus, a Greek philosopher (B.C.?-287), gave the first known description of the plant. From him we learn that the papyrus grew in shallows of 2 cubits (1 cubit = 18 or 20 inches) or less and that its main root was about 10 cubits long and of the thickness of a man's wrist. From this root, smaller roots branched out. The smooth stem of the plant, which contained only a cellular pith within the rind, grew to about 12 feet in height, tapering to a large drooping flower cluster.

The papyrus plant was put to many uses. The heads were used as garlands for decorating the shrines of the gods; the root was used for making various utensils and for fuel; the stem was used for making boats, sails, mats, cloth, cords, and especially writing material. The

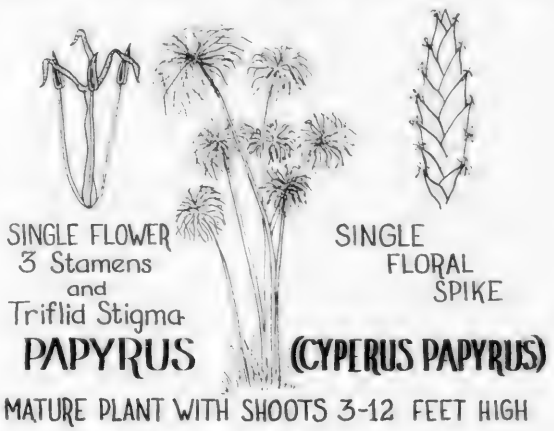


Fig. 1

Presented before the Ramazzini Society, Gaylord, Mich., Oct. 1, 1960.

pith was used as a food and was eaten both cooked and in its natural state.

The most extensive use of the papyrus plant was in the manufacture of writing materials. Besides this use in Egypt, the papyrus as writing material was known to the Ionian Greeks, who gave it the name "skin," after the vellum they were accustomed to using. There is evidence that it was used in Athens as early as the fifth century B.C. The papyrus was widely used under the Roman Empire because it was required for the production of books, for correspondence, and for legal documents.

From Pliny the Younger, we get our information in regard to the methods of manufacturing writing material from the papyrus. His description concerns the method employed in his own time; but doubtless the same method, with slight variations in detail, had been used through past generations. According to Pliny, the stem of the papyrus plant was cut in longitudinal strips—those from the center of the plant being the broadest and most valuable. The strips were laid side by side until the required width was reached. Across this layer, was placed another one of shorter strips, laid at right angles. These two layers formed a sheet which was then soaked in the waters of the Nile. The Nile, being thus specified, has caused much controversy among commentators. Some have thought that because a particular river was mentioned, it must contain some chemical property which acted as a glue to hold the two layers together. Other commentators say the material itself contained the substance which was dissolved by the action of water, whether from the Nile or elsewhere.

After the layers were soaked for a sufficient time, they were hammered to ensure flatness and to beat out as much moisture as possible, and then allowed to dry in the sun. *Recto* was the side on which the fibers ran horizontally, *verso* that on which the fibers ran vertically.

Even when work on the sheets of papyrus was completed, the material was not yet ready for use. It had to be made into a roll. To form a roll, 20 sheets were pasted together. Such a roll was called a "scapus." There are in existence, however, rolls consisting of more than 20 sheets; so the number may not have been constant. The scapus seems to have been a standard length sold by the stationers. The best sheet formed the first or outside part of the roll, and the others were joined on in order of quality so that the worst sheets were in the center.

Pliny also gives the classes of writing material (charta, or paper) and their sizes. They are as follows:

Old Egyptian Medical Papyri (from Leake)

Document	*Columns*	*Lines*	*Recipes*	*Date*
Papyrus Ebers	110	2,289	877	16th century B.C.
Papyrus Hearst	16	273	260	16th century B.C.
Berlin papyrus	24	279	204	16th century B.C.
London papyrus	19	253	63	11th century B.C.
Edwin Smith papyrus	21-½	377 (recto) 92 (verso)		17th century B.C. (copy of material 25th to 30th century B.C.)
Kahun (Kaehn) Gynecological papyrus	small fragment			20th century B.C.
Kahun veterinary fragment	....	....	....	20th century B.C.
Papyrus Brugsch minor	...	....	....	12th-14th century B.C. (?)

1. The *charta Augusta* was considered the best quality and was formed from the broadest strips of the plant. This class was originally called "*hieratica*," but the name was later changed to flatter Emperor Augustus. The *charta Augusta* was of such a fine and porous nature that it was not suited for literary purposes. It was reserved for correspondence only.

2. The *charta Livia*, named in honor of the emperor's wife, was 9½ inches in width, as was also the *charta Augusta*.

3. The *hieratica*, originally of the first class, was 8 inches wide.

4. The *charta Amphitheatrica* was named after the place of manufacture, the Amphitheatre of Alexandria, and was 6½ inches wide.

5. The *charta Fanniana* was a papyrus made up from the *charta Amphitheatrica* but was an inch wider, having been subjected to other flattening processes in the factory of a Roman named Fannius.

6. The *Saitica*, named from the city of Sais, was 5⅜ inches wide. This was a commoner type of papyrus.

7. The *Taeniotica* was named, apparently, from the place of manufacture—a tongue of land near Alexandria. It was sold by weight and varied in width from 4⅜ to 5 inches.

8. The *charta emporetica* was the common packing paper and was 4⅜ inches wide.

9. The *charta Claudia* was introduced during the reign of Claudius and was made from the *charta Augusta* and the *charta Livia*. A layer of the former was backed with a layer of the latter so that the width was increased to almost 12 inches.

10. The *charta macrocollon* was the largest of all the papyri. Eighteen inches wide, it was the size used by Cicero in his writings. Papyri of this width proved unpopular, however, because of the danger of injury by tearing.

An examination of existing papyri has shown

that sheets measuring about 12 inches often were used. A large class of them measure 10 inches. Others measure 8 inches, while the smaller ones range from 4 to 6 inches.

The Cyperus was cultivated in Egypt and manufactured into writing material down to the eighth and ninth centuries, when the paper industry began. With the manufacture of paper, the papyrus writing material was no longer a necessity and by the end of the 10th century it seems to have entirely disappeared.

As to Edwin Smith

Mr. Smith, after whom the papyrus of interest to Luckhardt is named, was a Connecticut Yankee born in 1822, the year in which Champollion began deciphering the Egyptian hieroglyphics. The celebrated Rosetta Stone, which supplied Jean François Champollion with the key for deciphering inscriptions on ancient Egyptian monuments, had been found near a town named Rosetta, near the western mouth of the Nile, by Boussard in 1799. It is a basalt stele inscribed in hieroglyphic, demotic, and Greek.

In Janaury, 1862, when Smith was offered a papyrus roll by a native named Mustapha Aga, he sensed its historical value and purchased it. Two months later he was offered another roll by the avaricious Mustapha Aga. The outer layer of the second roll consisted of several fragments of the papyrus originally purchased by Smith (presumably removed by the Egyptian tomb-robber and salesman of antiques in an effort to improve the appearance of the genuine article). Smith recognized the nature and probable value of the fragments glued to the spurious papyrus, negotiated a purchase, and in doing so no doubt supported the reputed gullibility of North Americans.

That Smith knew the medical nature of the content of the papyrus is evident in his notes. He made a remarkable attempt to translate it; was defeated by the limited knowledge of the Egyptian language possessed by scholars of the last century. After his death, in 1906, Smith's daughter presented the papyrus and the recovered fragments to the New York Historical Society. Later these documents were lodged with the Brooklyn Museum, and in December, 1948, were presented to the New York Academy of Medicine.

As to Hieroglyphic, Hieratic, and Demotic Symbols

James Henry Breasted in volume 1 of his "Hieroglyphic Text Translation and Commentary of the Edwin Smith Surgical Papyrus" has a section labeled "General Explanatory Notes for Physicians and Other Non-Egyptological Readers." From this section I now borrow liberally.

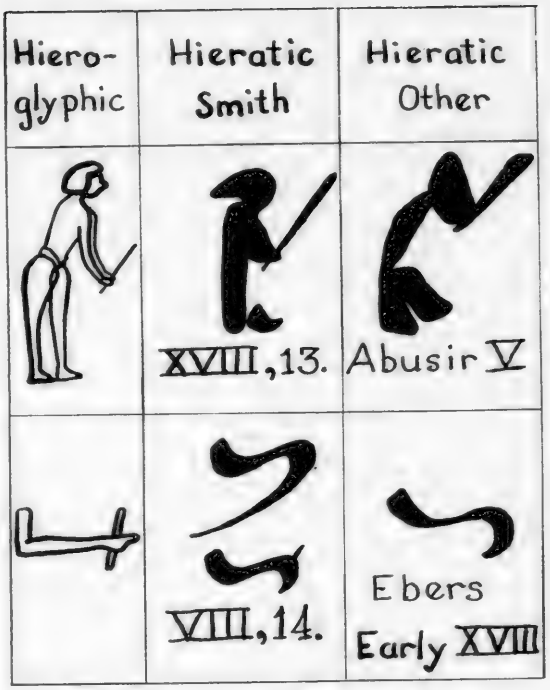


Fig. 2—Comparative paleographic forms.

Egyptian writing originally was purely pictographic. These pictures, or sketches of the thing represented, are called *hieroglyphs*. In an effort to speed up the representation of hieroglyphs in the pen and ink symbols on papyrus rolls, for the daily affairs of commerce, there appeared a more rapid, cursive form of signs known as *hieratic* (Fig. 2). The latter soon had but slight resemblance to pictographs. A similar development can be seen in our own handwritten use of the original uncials (capital letters) of our alphabet. For example, the capital *B* as presently written as a lower case (minuscule) *b* in handwriting retains the upper loop but leaves the lower loop incomplete as a timesaving device in moving on to the next letter of a word without lifting the pen. Long before 3000 B.C. the Egyptian scribes had resorted to the rapid hieratic handwritten form for daily business and government records; inscriptions on steles were carved in hieroglyphs.

A still later form of cursive script (abbreviated and simplified) came into use when hieratic was found to be too elaborate for quick writing. The later form is called *demotic*. While the development of the logograph (sym-

bol for a word) and phonetization (sound for a word, a contribution of the Sumerians), were important advances in communication, the development of the alphabet by the Greeks was even more significant.

The Edwin Smith Papyrus is written in hieratic (Fig. 3). The first step in its translation by Breasted was the preparation of a hieroglyphic "transliteration," comparable to a typewritten copy of the script (Fig. 4). Both versions are written right to left.

As to the Translator Breasted

An Associated Press news report of Dec. 2, 1935, read as follows:

Dr. James H. Breasted, noted archeologist and head of the Oriental Institute of the University of Chicago, died today.

Hospital authorities in announcing his death maintained the same secrecy as they had concerning his strange illness.

The archeologist was one of the discoverers of the tomb of King Tutankhamen on whose walls were engraved the words:

> "Death shall come on swift wings to him
> that toucheth the tomb of Pharoah."

Dr. Breasted had frequently ridiculed this curse. [The diagnosis was streptococcal septicemia.]

Years of research conducted and directed by Prof. James Henry Breasted made vivid personalities of monarchs, law givers and military leaders, dead for centuries.

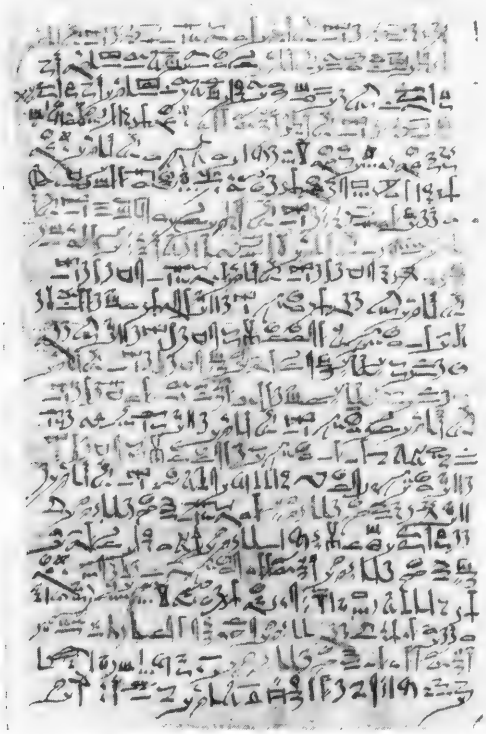


Fig. 3—The surgical treatise, Column XI.

Fig. 4—Hieroglyphic transliteration of Column XI.

Recognized as the leading Egyptologist of the United States and one of the foremost authorities in the world on ancient civilization, he also was a remarkably able organizer and administrator.

It was under the guidance of Professor Breasted that the Oriental Museum and Institute of the University of Chicago was made the center of research in America in recovering the lost chapters of the world's history represented in Egyptian, Hittite and other culture.

His interest in the past dated to the days of his boyhood in Rockford, Illinois, where he was born August 27, 1865, the son of Charles and Harriet Garrison Breasted. As a boy he eagerly read available material on Egypt and was fired with a desire to add to the record.

In his "The Conquest of Civilization," he told of being present at the site of ancient Armageddon where one of the University of Chicago expeditions was excavating that famed battlefield. One of the excavators dug out a block of stone bearing Egyptian hieroglyphics, which when deciphered was found to relate the conquests of Shishak, a Pharoah of the tenth century before Christ.

"Instantly," said Professor Breasted, "there rose before me the vision of a Sunday school in a little church on the far off prairie of Illinois, where nearly half a century ago a group of village boys with heads together over the Bible were struggling with the difficult proper names of an old Hebrew chronicle:

"And it came to pass in the fifth year of King Rehoboam that Shishak, king of Egypt, came up

against Jerusalem, and he took away the treasures of the house of Jehovah; and the treasures of the king's house; he even took away all; and he took away all the shields of gold that Solomon had made."

"It was with some emotion," he continued, "that one of these boys was reading the name of the old Egyptian conqueror who carried Solomon's treasure from Jerusalem nearly 3,000 years ago."

Prof. Breasted received an A.B. degree from Northwestern College of Naperville in 1888, studied between 1888-1890 at the Chicago Theological Seminary where he got his first knowledge of Hebrew, and then went to Yale for further work in Oriental languages, receiving his A.M. degree there in 1892. He received his doctor's degree at the University of Berlin two years later. Numerous honorary degrees, including that of Doctor of Literature from Oxford in 1922, were conferred upon him.

As to the Edwin Smith Surgical Papyrus

In the Foreword of Breasted's translation may be seen this comment: "When in 1920 I was requested by the New York Historical Society to translate and publish the papyrus, I was at first inclined to refuse, in view of heavy administrative responsibility for the affairs of the Oriental Institute. Imagine my surprise, however, when I saw the splendid folio columns of this magnificent papyrus manuscript! And when I had examined its contents even summarily, I was unable to refuse. . . . After interpreting the document as best I could with my limited knowledge of the human body, I handed the manuscript to my medical colleague, Dr. Arno B. Luckhardt, who very kindly undertook the burdensome task of looking it through and appending his suggestions. I have acknowledged these notes in their proper places, but I wish to express here my sincere appreciation of Dr. Luckhardt's valuable assistance."

Unrolled and mounted between glass, the Edwin Smith Papyrus has a length of 4.68 meters (about 15 ft. 3 in.). At least a column of writing has been lost at the beginning, so that it originally had a minimum length of 5 meters (about 16 ft. 4 in.). The roll has a height of 32½ to 33 cm (about 13 in.) corresponding to the usual full-height roll of the period from the Middle Kingdom through the Hyksos Age to the early Empire. It is put together out of twelve sheets of the usual size, about 40 cm. (15¾ in.) wide, the first now surviving being unfortunately fragmentary. The 11 joints are admirably done, and in its craftsmanship the roll is an excellent piece of work. It now bears 17 columns of writing on the recto and 5 on the verso, all in horizontal lines. The recto contains 377 lines and the verso 92. The entire front, 17 columns, and the first 3½ columns of the verso are the work of one hand. The concluding section is by a different and possibly somewhat later hand. The copy of the document which has come down to us dates from the seventeenth century B.C. The original author's first manuscript was written a thousand years or more earlier.

The scribe of the Smith Papyrus was guilty of a surprisingly large number of omissions, which he failed to notice or to bother about. He shows evidence of the fact that he was not himself a medical man. Often his mistakes require cancellation or change. In almost all cases he has detected these errors and has made his corrections in red ink over black, or in black ink over red. In one place he indicates the omission of a line by a cross (×) and inserted the necessary words at the top of the column of the hieratic script (Fig. 3). This presumably is the first use of the asterisk in literature.

Forty-eight case histories are presented, all injuries, or induced by injuries (with two possible exceptions). The discussion begins with the head and skull, proceeding thence downward by way of the nose, face and ears, to the neck, clavicle, humerus, thorax, shoulders, and spinal column, where the text is discontinued, leaving the document incomplete.

The discussion of each case discloses a systematic order of materials and topics—an arrangement which, with the exception of some elaboration in six cases, is strictly followed. The order is as follows: (1) Title; (2) Examination; (3) Diagnosis; (4) Treatment (unless a fatal case, considered untreatable); (5) Glosses (a little dictionary of obscure terms employed in the discussion of several cases). An elaboration of the above scheme (in cases 7, 8, 28, 34, 37, and 47) is due to the interesting fact that the surgeon's rceords disclosed an alternative group, or even more than one alternative group of symptoms, requiring in each case a different treatment, or demonstrating the certainty of a fatal outcome and hence followed by no suggestion for treatment. Case 7 is the longest case in the treatise.

The *Title* consists of the word signifying "Instructions," followed by the identifying designation of the injury, together with indication of the region or organ affected, and sometimes with additional details. Thus the title to Case 4 reads: "Instructions concerning a gaping wound in his head, penetrating to the bone, (and) splitting his skull."

The *Examination* is conceived as spoken by someone addressing a second person, who is regularly designated by a pronoun in the second person singular. The form of the examination

therefore is that of a teacher instructing a pupil that he shall do so and so. Grammatically, the examination is a long protasis, of which the diagnosis forms the apodosis. In other words, the examination is the first part of a long conditional sentence comprising a recital of the symptoms which it is assumed the surgeon has observed in the patient, and which form the basis of the resulting conclusions expressed in the diagnosis. The examination frequently begins thus: "If thou examinest a man having . . . " which is followed by the name of the injury or ailment already placed at the head of the discussion in title of the case.

The following methods of observation are either expressly stipulated in the text, or are clearly implied: (*a*) answers elicited from the patient by questions which the surgeon addresses to him (Case 22), (*b*) visual observations (Case 28), (*c*) olfactory observations, (*d*) tactile observations, as "Thou shouldst lay thy hand upon it" (the wound, Case 6 and Case 47) and (*e*) movements of parts of his body by the patient as directed by the surgeon, as "Thou shouldst cause him (the patient) to lift his face" (Case 7).

The *Diagnosis* is introduced by the words: "Thou shouldst say concerning him" (the patient), as if addressed to a student or young surgeon by the speaker. The concluding statement of the diagnosis consists of an utterance often in the first person, such as, (*A*) "One having . . . " (followed by the description of the ailment) or (*B*) "An ailment which I will treat," expressing his coming course of action toward the case. In the second part of the diagnosis the treatise classifies all cases under three categories, as (1) Treatable; (2) Possibly curable; and (3) Untreatable. These three verdicts are not prognoses. They are not so much statements regarding the cases, as they are the surgeon's declaration of his own future course of procedure and are indicated in translation as follows: (1) "An ailment which I will treat"; (2) "An ailment with which I will contend"; (3) "An ailment not to be treated."

In the 48 cases discussed there are 52 of these verdicts. Five cases contain two verdicts, varying as the surgeon's findings vary (Cases 7, 8, 34, 37, and 47). Case 9 contains no such verdict. The lack of this characteristic, together with the fact that the case contains no diagnosis of any kind, relegates this case to the class of magical recipes drawn from the recipe papyri employed by the recipe-vending physicians of the period. The third verdict is not found in any of the other medical documents of Egypt, although it occurs no less than 14 times in Papyrus Smith. One of these cases (17) has received this verdict by an evident error of the scribe. We have left, therefore, 13 instances to which the third verdict is correctly applied. Of these 13 cases, 10 contain no therapeutic suggestions whatever. Here is shown an interest in truth and in science for its own sake quite unprecedented and not observable elsewhere in any of the ancient documents of Egypt, whatever the character of their content.

The *Treatment*. In the 58 examinations there are 42 instances in which treatment is prescribed at some stage. Examples are (*a*) Exclusively mechanical or surgical treatment—(1) lint; (2) plugs or swabs of linen; (3) bandages made no doubt by that skillful bandagist of antiquity, the Egyptian embalmer; (4) adhesive plaster; (5) surgical stitching; (6) cauterization; (7) splints or braces; (8) supports of abode: (*b*) Combination of surgical treatment with the external use of medicaments: (*c*) Exclusive use of medicaments externally applied.

The *Glosses* (sixty-nine in number) form a valuable body of information in the papyrus. They constitute a little dictionary of terms distributed throughout the treatise, which was already so old in the Twenty-sixth Century B.C. that it contained numerous terms no longer current and hence requiring explanation. A commentator, as totally unknown to us as is our original author, has added his definitions and explanatory comments. He cannot have been the scribe who copied our papyrus. This worthy was far too careless, and betrays his ignorance of medical science far too obviously to have been able to produce such a remarkable little dictionary. In twenty-nine out of our forty-eight cases, it was found necessary to add one or more of these explanatory glosses, making altogether a total of sixty-nine. Each gloss is invariably introduced by "as for" or "with regard to" followed by a verbatim quotation of the word or phrase to be explained, and concluding with "it means" and the explanation (Cases 6, 22, and 31). A common designation for sinew, muscle, and perhaps also for nerve, arises in that nerves, blood vessels and muscles were not clearly recognized as three separate systems.

The author of this document knew that in observing the character of the pulse he was learning something of cardiac function. He affirmed that there is a canal leading from the heart to every member of the body, and adds that its "pulsation is in every vessel of every member." The ancient writer states clearly that observations on the pulse are undertaken "in

order to know the action of the heart." Luckhardt concluded that the author "must have noted that the apex beat and the pulsation of the peripheral arteries were roughly synchronous and therefore that the rate, volume, and the regularity of the latter were roughly an index of the state of functional activity of the former."

The bony framework of the body was familiar to the Egyptian. The fork at the summit of the ramus of the mandible is compared to the claw of a two-toed bird (Case 22). The calvarium is likened to a turtle's shell and a hole in the skull, to a hole broken in a pottery jar.

For the first time in recorded human speech the word "brain" appears (it is not found again until 2,000 years later, when it is identified in Greek medical documents). The rugae of the brain are noted to resemble the corrugations on metallic slag (Case 6). In a case of compound comminuted fracture of the skull the Egyptian writer describes rupture of the "sack containing the brain," an obvious reference to the meninges. He also notes that brain injuries can produce paralysis of a lower extremity; however, no doubt influenced by a case of contrecoup fracture and brain injury, he localized brain injury and paralysis on the same side of the body. The ancient writer recorded the fact that after a cervical dislocation the injured man exhibited a penile erection and a seminal emission (Case 31).

The scribe of the 17th century B.C. who was copying the material found in the older document was little aware of the momentous decision he was making when he pushed aside the ancient treatise; stopping in the middle of a line, in the middle of a sentence, in the middle of a word. In this act our generation lost the remainder of this remarkable scientific work.

The characteristics of this papyrus which distinguish it from other medical papyri are the following: (1) It is a surgical treatise and the oldest known such document. (2) It consists of case histories, not recipes and incantations characteristic of other medical papyri. (3) It is systematically organized, starting with head injuries and moving down the body structure. (4) The observations reported are objective, the treatment rational and scientific. (5) Each case is given one of three verdicts: favorable, uncertain, or unfavorable.

The verdict "an ailment not to be treated" appears in no other known Egyptian treatise. Here is evidence of scientific interest in the phenomena disclosed by medical examination with a mention of conclusions based on observable facts.

The cases were chiefly injuries resulting from trauma. From where did such clinical material come? Undoubtedly from the occupational hazards of building pyramids and carrying spears into battle for the Pharoahs. The patient is always a man. This then appears to be our oldest text on occupational injuries and traumatic surgery.

The treatise was written in the Old Kingdom (3000 to 2500 B.C.), presumably in the early part of that remote age. There is no hint at the name or station of the author. He was obviously a remarkable man of his day, at least in his knowledge of human anatomy, physiology, and conservative surgery. It seems likely that he practiced dissection of the human body.

If we wish to make a conjecture, as Breasted has pointed out, is this treatise the work of that genius, adumbrated by time, Imhotep?

Imhotep, the Son of Ptah, and the physician and architect to Pharoah Zoser (*ca.* 2980-2900 B.C.) is credited with designing the Step-Pyramid of Sukkarah, and has come down through history, via monuments and funerary papyri, by virtue of his many accomplishments and his posthumous deification. Imhotep has been described as "Giver of Life . . . who provides remedies for all diseases"; "He who never sleeps night or day"; "The divine falcon"; "Imhotep the Great One"; "Son of Ptah." William Osler refers to Imhotep as "the first figure of a physician to stand out clearly from the mists of antiquity." Numerous surviving bronze votive statuettes (12 to 20 cm high) are of the figure of Imhotep, cast many centuries after he lived. Imhotep became a demigod about 1580 B.C.; was ranked among the full gods of Egypt in the Persian period, dating from 525 B.C. In becoming the Egyptian god of medicine he preceded Asklepios (the Grecian god) by several centuries.

The record shows that Imhotep grew up as an erudite and versatile man who took all knowledge as his province, in an Aristotelian manner. Sources have identified him as serving the Pharoah as (1) grand vizier, (2) architect, (3) chief lector priest or ritualist, (4) sage and scribe, (5) astronomer, and (6) physician.

Because of the timing of his life and the undoubted influence he had about 3000 B.C., it is a pleasant conjecture to credit Imhotep with a textbook on the surgery of trauma which circulated among Egyptian physicians when the Great Pyramid of Gizeh was being built.

In the Papyrus Ebers there is an isolated passage on the heart which is said to be quoted

from another ancient medical book entitled "Secret Book of the Physician." This same passage on the heart, quoted in Papyrus Ebers, is also found in the Edwin Smith Papyrus, and, according to Breasted, "has every appearance of being original there." Thus, there is evidence that the treatise which constitutes currently our earliest text on industrial or military surgery was known to its ancient users as the "Secret Book of the Physician." Somewhat later (28th century B.C.) than the probable genesis of the case reports found in the Edwin Smith Papyrus the chief architect Weshptah to Pharoah Neferir Kere had a stroke. The ancient inscription in which the incident is recorded states "His majesty had brought for him a case of writings . . . They said to his majesty that he was unconscious." This case of writings may have been the material copied, in part, in the Smith Papyrus.

Conclusion

The most astounding thing about these case histories is that we find so little reference to incantations and appeals to supernatural powers to heal the sick man. Other references to ancient and even medieval medical treatment of a patient regularly imply the concept that a sick man is obsessed by demons. This remarkable surgeon-author peers into the mysteries of the human body and concerns himself with intelligible physical causes of disease in a brilliant fashion. And he does this in the midst of a superstitious society 5,000 years ago! He discovers the brain, recognizes the relation of the beating heart to the pulse, and knows the function of bones and ligaments. Such findings impress the present-day reader with the remarkableness of the height of civilization, accumulation of knowledge, and preservation of records of the long hidden early Egyptian society.

Illustrated Cases

Case 6 (II 17-III 1)
A Gaping Wound in the Head with Compound Comminuted Fracture of the Skull and Rupture of the Meningeal Membranes

Title—Instructions concerning a gaping wound in his head, penetrating to the bone, smashing his skull, (and) rending open the brain of his skull.

Examination—If thou examinest a man having a gaping wound in his head, penetrating to the bone, smashing his skull, (and) rending open the brain of his skull, thou shouldst palpate his wound. Shouldst thou find that smash which is in his skull [like] those corrugations which form in molten copper, (and) something therein throbbing (and) fluttering under thy fingers, like the weak place of an infant's crown before it becomes whole—when it has happened there is no throbbing (and) fluttering under thy fingers until the brain of his (the patient's) skull is rent open—(and) he discharges blood from both his nostrils, (and) he suffers with stiffness in his neck, (conclusion in diagnosis).

Diagnosis—[Thou shouldst say concerning him]: "An ailment not to be treated."

Treatment—Thou shouldst anoint that wound with grease. Thou shalt not bind it; thou shalt not apply two strips upon it: until thou knowest that he has reached a decisive point.

Gloss A—As for: "Smashing his skull, (and) rending open the brain of his skull," (it means) the smash is large, opening to the interior of his skull, (to) the membrane enveloping his brain, so that it breaks open his fluid in the interior of his head.

Gloss B—As for: "Those corrugations which form on molten copper," it means copper which the coppersmith pours off (rejects) before it is [forced] into the [mould], because of something foreign upon it like [wrinkles]. It is said: "It is like ripples of pus." (Breasted,[2] vol. 1, pp. 434-435)

Case 22 (VIII 9-17)
Compound Comminuted Fracture of the Temporal Bone

Title—Instructions concerning a smash in his temple.

Examination—If thou examinest a man having a smash in his temple, thou shouldst place thy thumb upon his chin (and) thy finger upon the end of his ramus, so that the blood will flow from his two nostrils (and) from the interior of his ear having that smash. Cleanse (it) for him with a swab of linen until thou seest its fragments (of bone) in the interior of his ear. If thou callest to him (and) he is speechless (and) cannot speak, (conclusion follows in diagnosis).

Diagnosis—Thou shouldst say concerning him: "One having a smash in his temple; he discharges blood from his two nostrils and from his ear; he is speechless; (and) he suffers with stiffness in his neck. An ailment not to be treated."

Gloss A—As for: "The end of his ramus," it means the end of his mandible. The ramus ('m'·t), the end of it is in his temple just as the claw of an 'am'e-bird ('m') grasps an object.

Gloss B—As for: "Thou seest its fragments (ws·t) in the interior of his ear," it means that some of the fragments (ws·t) of the bone come away to adhere to the swab which was introduced to cleanse the interior of his ear.

Gloss C—As for: "He is speechless," it means that he is silent in sadness, without speaking, like one suffering with [feebleness] (dgy) because of something that has entered from outside.
(Breasted,[2] vol. 1, pp. 447-448)

Case 28 (IX 18-X 3)
A Gaping Wound in the Throat Penetrating to the Gullet

Title—Instructions concerning a wound in his throat.

Examination—If thou examinest a man having a gaping wound in his throat, piercing through to

his gullet; if he drinks water he [chokes] (and) it comes out of the mouth of his wound; it is greatly inflamed, so that he develops fever from it; thou shouldst draw together that wound with stitching.

Diagnosis—Thou shouldst say concerning him: "One having a wound in his throat, piercing through to his gullet. An ailment with which I will contend."

First Treatment—Thou shouldst bind it with fresh meat the first day. Thou shouldst treat it afterward [with] grease, honey, (and) lint every day, until he recovers.

Second Examination—If, however, thou findest him continuing to have fever from that wound, (conclusion in following second treatment).

Second Treatment—Thou shouldst apply for him dry lint in the mouth of his wound, (and) moor (him) at his mooring stakes until he recovers.

(Breasted,[2] vol. 1, p. 451)

CASE 31 (X 12-22)

DISLOCATION OF A CERVICAL VERTEBRA

Title—Instructions concerning a dislocation in a vertebra of [his] neck.

Examination—If thou examinest a man having a dislocation in a vertebra of his neck, shouldst thou find him unconscious of his two arms (and) his two legs on account of it, while his phallus is erected on account of it, (and) urine drops from his member without his knowing it; his flesh has received wind; his two eyes are blood-shot; it is a dislocation of a vertebra of his neck extending to his backbone which causes him to be unconscious of his two arms (and) his two legs. If, however, the middle vertebra of his neck is dislocated, it is an *emissio seminis* which befalls his phallus.

Diagnosis—Thou shouldst say concerning him: "One having a dislocation in a vertebra of his neck, while he is unconscious of his two legs and his two arms, and his urine dribbles. An ailment not to be treated."

Gloss A—As for: "A dislocation (wnh) in a vertebra of his neck," he is speaking of a separation of one vertebra of his neck from another, the flesh which is over it being uninjured; as one says, "It is wnh," concerning things which had been joined together, when one has been severed from another.

Gloss B—As for: "It is an *emissio seminis* which befalls his phallus," (it means) that his phallus is erected (and) has a discharge from the end of his phallus. It is said: "It remains stationary" (mn s'w), when it cannot sink downward (and) it cannot lift upward.

Gloss C—As for: "While his urine dribbles," it means that urine drops from his phallus and cannot hold back for him. (Breasted,[2] vol. 1, pp. 465-466)

CASE 47—(XVI 16-XVII 15)

A GAPING WOUND IN THE SHOULDER

Title—Instructions concerning a gaping wound in his shoulder.

First Examination—If thou examinest a man having a gaping wound in his shoulder, its flesh being laid back and its sides separated, while he suffers with swelling (in) his shoulder blade, thou shouldst palpate his wound. Shouldst thou find its gash separated from [-] its sides in his wound, as a roll of linen is unrolled, (and) it is painful when he raises his arm on account of it, thou shouldst draw together for him his gash with stitching.

First Diagnosis—Thou shouldst say concerning him: "One having a gaping wound in his shoulder, its flesh being laid back and its sides separated, while he suffers with swelling in his shoulder blade. An ailment which I will treat."

First Treatment—Thou shouldst bind it with fresh meat the first day.

Second Examination and Treatment—If thou findest that wound open and its stitching loose, thou shouldst draw together for him its gash with two strips of linen over that gash; thou shouldst treat it afterward [with] grease, honey, (and) lint every day until he recovers.

If thou findest a wound, its flesh laid back, its sides separated, in any member of a man, thou shouldst treat it according to these directions.

Third Examination—If, however, thou findest that his flesh has developed inflammation from that wound which is in his shoulder, while that wound is inflamed, open, and its stitching loose, thou shouldst lay thy hand upon it. Shouldst thou

H h

find inflammation issuing from the mouth of his wound at thy touch, and secretions discharging therefrom are cool like *wenesh*-juice, (conclusion follows in second diagnosis).

Diagnosis Following Third Examination—Thou shouldst say concerning him: "One having a gaping wound in his shoulder, it being inflamed, and he continues to have fever from it. An ailment with which I will contend."

Fourth Examination—If then, thou findest that man continuing to have fever, while that wound is inflamed, (conclusion in following treatment).

Treatment Following Fourth Examination—Thou shalt not bind it; thou shalt moor (him) at his mooring stakes, until the period of his injury passes by.

Fifth Examination—If, however, his fever abates and the inflammation in the mouth of his wound dissipates entirely, (conclusion in following treatment.

Treatment Following Fifth Examination—Thou shouldst treat him afterward [with] grease, honey, (and) lint every day, until he recovers.

(Breasted,[2] vol. 1, pp. 465-466)

(The author's address is Hercules Tower, 910 Market St., Wilmington 98, Del.)

References

1. Encyclopaedia Britannica, 1947, Vol. 17, pp. 246-248.

2. Breasted, J. H.: The Edwin Smith Surgical Papyrus, (Chicago), University of Chicago Press, 1930.

3. Hurry, J. B.: Imhotep, The Vizier-Physician of King Zoser and Afterward The Egyptian God of Medicine, Oxford, Oxford University Press, 1926.

4. Leake, C. D.: The Old Egyptian Medical Papyri, (Lawrence, Kan.) University of Kansas Press, 1952.

DETERMINANTS OF

Ischemic Electrocardiographic Abnormalities and Chest Pain

Part II—The Exercise Electrocardiogram Test

Richard Gubner, M.D., New York, N.Y.

IN A PREVIOUS report in this JOURNAL[26] the applications, significance, and criticisms of the exercise electrocardiogram test in detecting coronary insufficiency were surveyed. The most direct method for demonstrating coronary artery disease, and one which has rapidly gained clinical status, particularly in context to potential surgical intervention such as endarterectomy, is contrast coronary arteriography using cineangiographic techniques. However, general clinical employment dictates a simpler method, for which the double two step exercise test serves quite adequately. Indeed, the electrocardiographic response to stress in many ways bears more closely on the problems of coronary insufficiency and angina pectoris than do morphologic changes in the coronary arteries, such as may be elegantly visualized by coronary arteriography. It is well recognized, that no necessary, or at times even close correlation obtains between organic changes in the coronary arteries and myocardial involvement or between these and electrocardiographic changes and anginal pain.[27]

Nature of Ischemic Electrocardiographic Abnormalities and Chest Pain

S-T segmental changes in the electrocardiogram after exercise, properly interpreted, are pathognomonic of myocardial ischemia, and are determined by the same factors responsible for chest pain, which is a frequent but not invariable concomitant of coronary insufficiency. Anatomically the portion of the heart muscle most vulnerable to ischemia is the subendocardial layer of the left ventricle including the papillary muscles, where the efficiency of coronary flow is lower than it is to the atria, right ventricle, and outer wall of the left ventricle. Intramural pressure in the left ventricle during systole, which is highest in the inner layer of the left ventricle, impedes coronary flow to the deeper layers of the left ventricle; but not to the outer left ventricular wall, right ventricle or atria, where intramural pressures are lower than coronary artery perfusing pressure. Accordingly, during the systolic portion of the cardiac cycle—and this becomes more significant the more rapid the heart rate—blood flow to the inner left ventricle is relatively compromised, explaining the predilection of this area to ischemic myocardial involvement.[28] Particularly is this the situation when significant coronary artery narrowing exists, and the coronary artery perfusion pressure is accordingly lowered. Involvement of the subendocardial portion of the left ventricle is reflected in the electrocardiogram as depression of the S-T segment. Depression of the S-T segment is produced experimentally[29, 30] as well as clinically by injury to the subendocardial region of the left ventricle, and this is the locus of the predominant biochemical as well as morphological lesion in coronary insufficiency and angina pectoris.[31]

Functionally (and the myocardial lesion of coronary insufficiency and angina pectoris is, except when severe and protracted, a reversible biochemical one rather than structural), the specific cause of the S-T depression abnormalities in the electrocardiogram, and also the determinant of anginal pain, is an acute potas-

Dr. Gubner is Medical Director, Diagnostic Services Division, Equitable Life Assurance Society of the United States, and Director of Medicine, Service A, Kings County Hospital Center, Brooklyn, N.Y.

The first article of this study was published in the February, 1960, issue of this Journal, pp. 57-61.

Submitted for publication Dec. 16, 1960.

sium efflux from myocardial cells caused by ischemia. If this potassium shift is minimized by preloading patients with coronary insufficiency with an infusion of potassium chloride prior to performance of exercise, S-T segmental depression and development of pain both may be prevented, as illustrated in Fig. 1. Conversely, if exercise is carried out after depleting myocardial potassium by infusion of sodium lactate, S-T segment abnormalities and pain on performance of exercise are both greatly enhanced. Indeed, infusion of sodium lactate may be used as a substitute for the exercise test when exercise cannot be carried out, and rapid infusion of 120 cc of molar sodium lactate will frequently produce anginal attacks and S-T segmental changes identical with those produced by exercise (Fig. 2). Since the factor of anoxia is not involved in this procedure, and similar ischemia prevails if exercise is carried out with or without pretreating with potassium chloride or sodium lactate, oxygen lack cannot be the cause of electrocardiographic abnormalities and pain sui generis.

The "P," or pain substance postulated by Sir Thomas Lewis, appears to be not an organic metabolite such as lactic acid, as has commonly been assumed, but rather the potassium ion. Efflux of potassium from the myocardial cell, which is the immediate and prime biochemical change to follow anoxia,[34, 35] leads to depletion of intracellular potassium.[36–38] Since the augmented extra cellular potassium is not promptly washed away owing to decreased coronary flow, the result is a greatly increased extracellular to intracellular potassium ratio. This is the physiological determinant of muscle contracture (treppe), i.e., sustained contraction, which occurs in heart muscle as well as in skeletal muscle.[39]

In this sense then, spasm of the affected myocardium occurs, and there is a substantive basis

Fig. 1—S-T and T changes and anginal attacks produced by Na lactate, and by exercise; prevention of electrocardiographic changes and pain by pretreatment with potassium chloride before exercise: (a) control; (b) Na lactate produced marked S-T and T changes and severe anginal attack, requiring six 1/150 grain glyceryl trinitrate (nitroglycerin) pills over 20 minutes before pain abated; (c) exercise test (single Master test) produced marked S-T and T changes and anginal attack; and (d) exercise test after pretreatment with KCl (30 mEq in 500 cc. 5% G in W in 40 minutes) did not produce electrocardiographic changes or pain (woman, 52, severe angina pectoris).

for the concept of myocardial spasm as the cause of angina pectoris, an early view which has not been held in repute for over a hundred years. There are relatively few pain fibers in the myocardium directly, and a further factor contributing to the sensation of pain may be spasm of the coronary veins, since a large outpouring of potassium occurs into the coronary veins from the myocardium immediately after the onset of ischemia.[34, 35] When total coronary occlusion occurs, there is a very large piling up of extracellular and coronary venous potassium, due to tissue release and failure of flow to wash it away, and prolonged pain, which characterizes acute myocardial infarction, results. This large accumulation of extracellular potassium is an important factor in causing ventricular arrhythmias and sudden death in coronary occlusion.[35] Electrocardiographically, extracellular potassium accumulation is reflected in abnormally tall pointed T waves which may be seen as the very earliest electrocardiographic change in acute coronary artery occlusion. An increased T wave amplitude is also commonly seen in tracings made immediately after exercise, at a time when increased potassium efflux, which is an accompaniment of increased work of the heart, has not yet been washed away by coronary flow. The effect of potassium in causing vascular spasm may be easily demonstrated by antecubital intravenous injection of potassium chloride at a flow rate exceeding 2 mEq per minute, which causes immediate spasm and pain along the subclavian vein.

Although the locus of electrocardiographic changes and pain appears to lie in myocardial

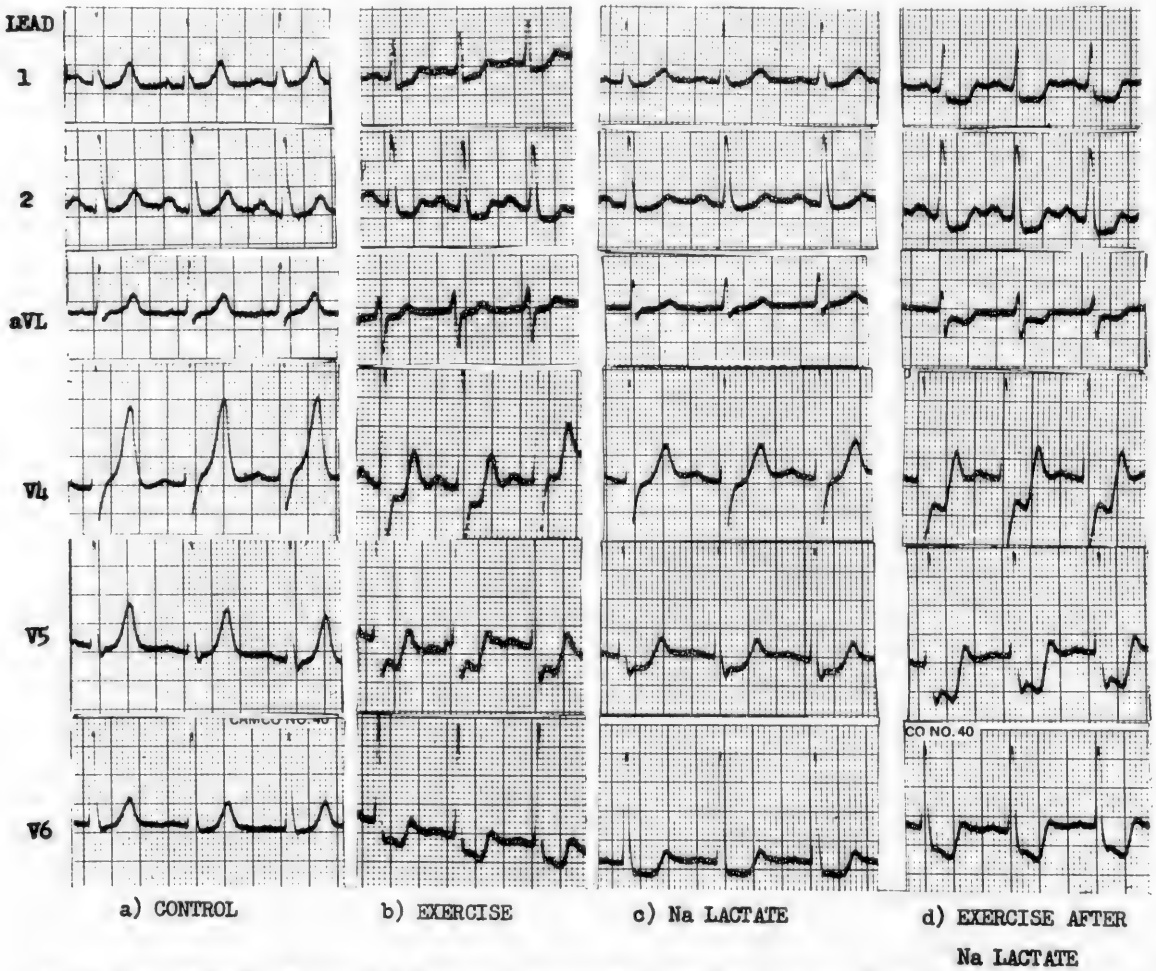


Fig. 2—Intensification of ischemic S-T changes produced by exercise by infusion of Na lactate prior to exercise: (a) control; (b) exercise (double 2-step) produced anginal pain and S-T abnormalities typical of acute coronary insufficiency; (c) Na lactate infusion produced S-T changes similar to those induced by exercise; (d) exercise performed after Na lactate infusion produced extreme S-T depressions, exceeding those resulting from exercise or Na lactate alone (man, 61, old posterior infarct, severe angina pectoris).

electrolyte changes, the primary lesion of myocardial ischemia which produces these changes is, of course, a serious compromise in coronary artery flow. Here too, however, functional factors superimposed on the morphologic lesions of narrowed coronary arteries are at play. A mechanistic view is generally held that coronary insufficiency results when there is a disproportion between myocardial oxygen needs and coronary artery oxygen supply; and augmented cardiac work with effort which cannot be compensated by a commensurate increase in coronary flow is generally held responsible for coronary insufficiency and angina pectoris. While this is doubtless true, the factor of increased cardiac work alone does not explain all the provocative factors in angina pectoris.[40] Notably may be mentioned the almost immediate occurrence of pain in some persons with acceleration of the heart rate and, conversely, the abrupt abatement of pain when the heart rate is slowed by carotid sinus pressure during an anginal attack (Fig. 3).

When the velocity of blood flow is accelerated, as happens immediately with tachycardia, lateral pressure against the arterial wall is decreased according to the Bernoulli principle, and if a coronary vessel is narrowed its opposing sides may be brought into apposition by the phenomenon of flitter. The hydraulic studies of Rodbard[41] on flow through collapsible tubes may be cited to illustrate this effect. "The presence of a partial constriction in the tube introduces new characteristics which markedly affect the conditions of flow . . . with stroboscopic illumination or high speed cinematography the smooth stream can be seen to be converted from an intact continuous column into a series of discreet drops . . . The production of an area of narrowing of a rubber segment sets the stage for an increased velocity and a consequent fall in lateral pressure, in the narrowed region. With the fall in lateral pressure, the walls of the rubber segment tend to collapse and this creates the conditions for a higher velocity, a further drop in lateral pressure, and progressive closure. When the tube is almost completely collapsed by this process, flow ceases and the total head becomes available as lateral pressure. This force blows the tube open, flow begins again, and the flitter cycle is repeated."

The cyclic nature of flow in the coronary arteries would appear to offer conditions particularly predisposing to flitter in critically narrowed coronary vessels. Accordingly, transient complete obstruction of a partially obstructed coronary artery may result. The cause of this transient obstruction lies in the accelerated flow rate within the vessel, rather than an active vascular constriction, but the effect is similar to that which would be produced by active coronary artery "spasm," a long mooted and improbable occurrence, since under conditions of anoxia coronary vasodilatation rather than

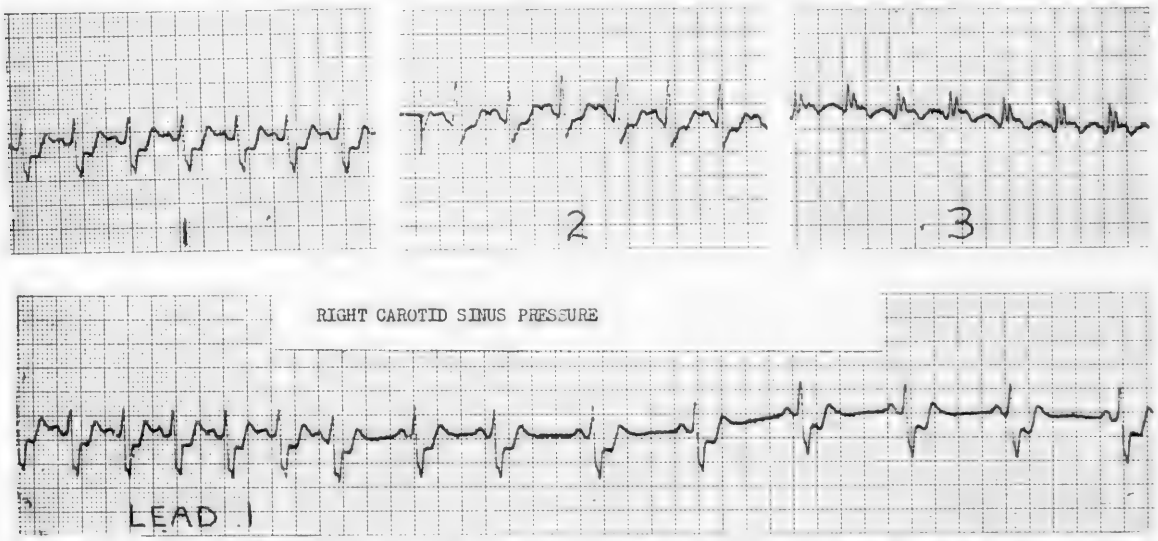


Fig. 3—Anginal attack, aborted by carotid sinus pressure. The patient, a man of 61, had had angina pectoris for 23 years, usually associated with a rapid heart rate. Leads I, II and III are recorded during a spontaneous anginal attack, at which time the heart rate was 138 per minute. Right bundle branch block is present, with depression of the S-T in Leads I and II. Carotid sinus pressure gave immediate relief from pain, although the S-T changes persisted for several minutes. It is usual for S-T changes to appear earlier than pain and to outlast the anginal attack. The patient was placed on reserpine, which slowed the heart rate, and a marked decrease in the frequency of anginal episodes resulted.

constriction occurs. Reducing the rate of flow by slowing the heart rate, or by enlarging the entire vascular bed with glyceryl trinitrate (nitroglycerin) ends the flitter effect, allowing return of coronary flow. Relief from angina pectoris which may follow induced hypothyroidism also may be attributed to a slowed velocity of blood flow eliminating flitter.

That coronary flow in a narrowed artery may actually be totally suspended during an anginal attack is illustrated in a case studied by Sones.[42] In this patient who had an attack of angina pectoris during coronary cineangiography transient complete shutdown of flow occurred through a diseased right coronary artery. The heart rate was considerably accelerated during the episode and a flitter phenomenon rather than active spasm may be presumed to have occurred. Patients with coronary artery disease extract more oxygen from their coronary circulation than do normal subjects, as reflected by more complete desaturation of coronary venous blood sampled from the coronary sinus.[43] A noteworthy exception, observed in two patients with angina pectoris who developed anginal attacks during effort studied by Gorlin,[43] was that both failed to demonstrate a fall in coronary venous oxygen content at the time of their pain. This may be explained by the interpretation offered above that total coronary artery flow cut-off occurred in the diseased vessels during the anginal attack and consequently the coronary sinus was not receiving blood from the affected portion of the myocardium.

There are other determinants of angina pectoris and coronary insufficiency that a straightforward mechanistic view of cardiac work in relation to coronary flow does not explain. Notable is the effect of food and insulin in potentiating or producing angina and ischemic electrocardiograph abnormalities. This may be attributed to a depletion of potassium from the heart[44] and serum produced by postprandial potassium movement and deposition in the liver. A common denominator of other factors which augment angina and electrocardiographic abnormalities also lies in their effect in depleting myocardial potassium, among them epinephrine, digitalis, and cold. Conversely, quinidine, which augments intramyocardial potassium,[45, 46] has been reported to ameliorate angina pectoris.[47]

The absence of pain in many persons with frank coronary insufficiency and even acute infarction, particularly in older persons, in women, and in persons with heart failure, finds an explanation in the considerably decreased myocardial potassium in women as compared

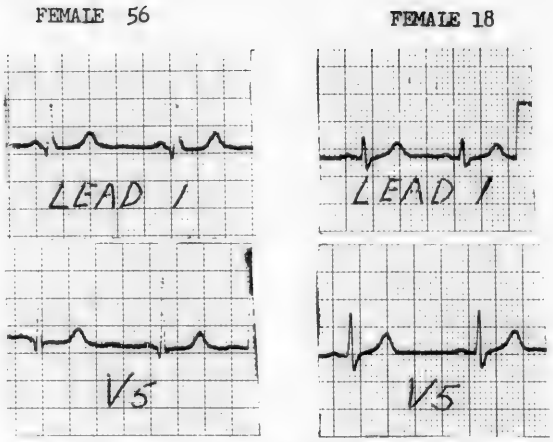


Fig. 4—"Older female" electrocardiogram. Leads I and V_5, are shown in a normal woman of 56, and a normal young woman, of 18. Note that the S-T segment is flattened, prolonged, and very slightly depressed in the older female, whereas in the younger woman the S-T tends to take off above the isoelectric line, with a rising and shorter limb. This difference presumably is due to decreased total body and myocardial potassium in older persons, particularly women. Exercise tests in older women very frequently exhibit "false positive" responses. Similar patterns and abnormal S-T changes with exercise may be observed in hypertension.

with men,[48] in older age groups[48] of both sexes, and in persons with heart failure. With the myocardium thus depleted of potassium, ischemia cannot provoke the acute marked potassium efflux which is the cause of pain, although the electrocardiographic abnormalities of ischemia are still evident in the form of S-T changes.

False Positive Exercise Tests and Criteria of Abnormality

The above consideration of the determinants of S-T segmental changes in the electrocardiogram and angina pectoris are pertinent to a discussion of the exercise test, for they help to explain the close association between the S-T changes and angina pectoris, which the exercise test is primarily used to authenticate. Futhermore, the observations concerning the basic role of potassium bear importantly on the question of false positive tests, which are frequently invoked as a criticism of the test. Any circumstance which depletes the myocardium and particularly the inner wall of the left ventricle, of potassium, be it tachycardia, a meal, age, female sex, digitalis, anxiety with epinephrine release, hypertension, or myocardial disease, will tend to lower the S-T segment. The pattern of the S-T segment in the resting electrocardiogram shows characteristic differences in older persons, particularly in women in whom total

body and myocardial potassium are most lowered, compared with the younger population. This may be recognized as a slightly depressed and relatively prolonged flat S-T segment, in contrast to the S-T in young persons, which is shorter and slopes upward into the T wave at a more obtuse angle (Fig. 4). When exercise is performed, these changes become more evident and a "positive" test is more readily elicited. Consequently, one cannot hope for specificity in the exercise test, however refined the criteria employed, in older persons and particularly in women much above the age of 40. Since coronary disease is a problem only in postmenopausal women, the test is of limited value unless striking changes result. Another important area of false positive tests, first pointed out by the author many years ago,[19] is

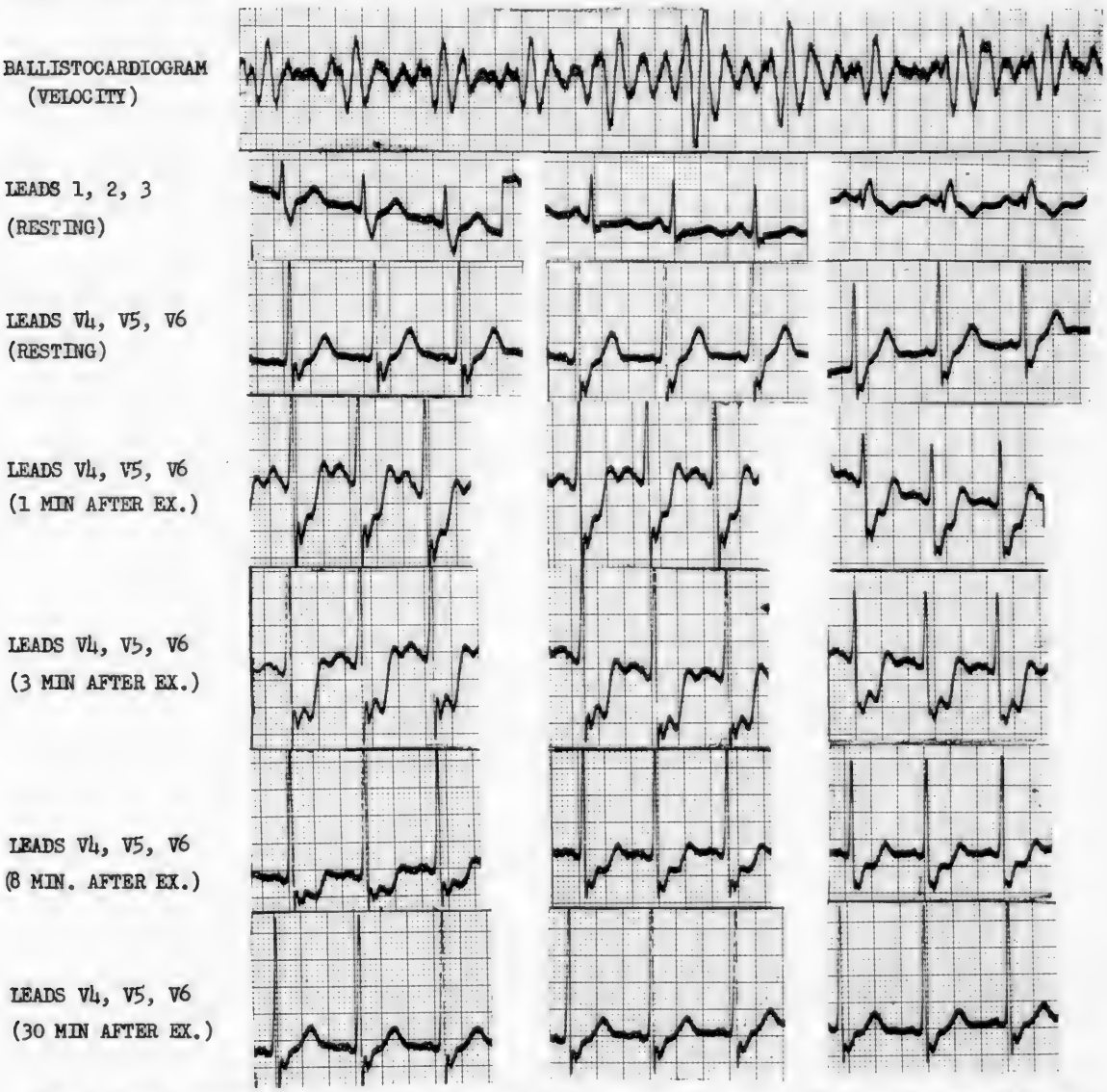


Fig. 5—Severe coronary insufficiency with marked S-T changes after exercise. The patient, a man of 57, had had chest pain on effort, and at times at rest, for five weeks. Resting tracing shows right bundle branch block. After 32 ascents chest pain developed and exercise was stopped. Chest leads V_4, V_5, and V_6 exhibit marked S-T abnormalities, which did not disappear until a half-hour after exercise. The patient was hospitalized and given anticoagulants because of concern over an impending infarct. The further course was uneventful. Tracings after exercise reveal coronary insufficiency in the presence of right bundle branch block, but are not informative with left bundle branch block. The ballistocardiogram (shown in top strip) was normal in all respects, with minimal respiratory variation. It is apparent that in this patient with severe coronary insufficiency the resting ballistocardiogram gave no clue to the presence of disease.

in persons who hyperventilate, in those of asthenic build, and in those who are anxious and may exhibit tachycardia.[50] In such situations S-T changes may occur which are of functional rather than organic origin, but they may ordinarily be distinguished from those of ischemic nature by their upward slope, to which the term junctional S-T has been applied, in contrast to the flat or sagging S-T segmental changes of ischemic nature.[51] Such functional S-T changes tend to be maximal in the immediate postexercise tracing, whereas those of ischemic origin usually are maximal in the two- to three-minute postexercise electrocardiogram. Positive exercise tests are also frequently elicited in persons with hypertension,[52] particularly those who have been on a salt-depleting regimen with thiazide diuretics causing potassium depletion. Digitalis likewise tends to favor a positive exercise test and it is of little value to carry out an exercise test in persons who have been receiving digitalis. Factors provoking "false positive" tests and features distinguishing such responses from true positive

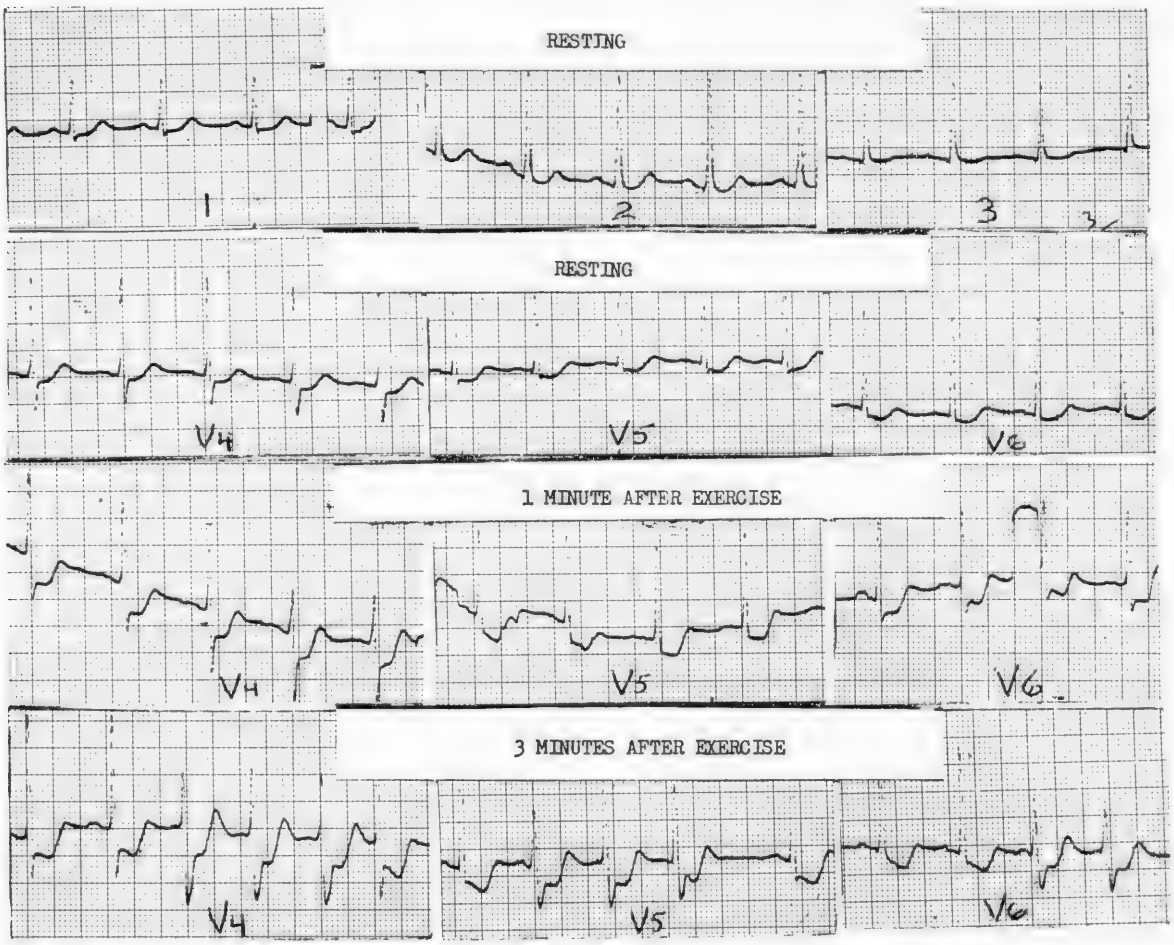


Fig. 6—Coronary insufficiency, with S-T changes in resting tracing, and arrhythmia after exercise. The patient, a male physical training teacher of 43, had had angina pectoris for two years. He was an exceedingly apprehensive patient and developed chest pain on excitement, or on slight effort when tense. However, when relaxed he had been able to perform much greater activity and could carry out gymnastics and other sports with little pain. The resting tracing, made at a time of tension, shows S-T depression in limb and precordial leads suggestive of coronary insufficiency. Tracing after double two-step exercise test shows marked increase in S-T segment abnormalities, and runs of supraventricular ectopic beats. Death occurred suddenly three weeks after this record. The presence of S-T changes in a resting tracing, marked increase in abnormalities with exercise, and increasing frequency of anginal attacks, all of which were present in this patient, are suggestive of impending infarction. Because of the history of peptic ulcer, anticoagulants were not employed. Similar fatal outcome in other patients observed by the author where anticoagulants were withheld because of a history of ulcer has suggested that prophylactic anticoagulants should be used despite such history.

tests have been surveyed by Lepeschkin and Surawicz.[53]

In general the more marked the S-T changes, the longer they persist (usually they are maximal in the two- to three-minute post-exercise period and tend to disappear by six minutes), the greater the number of leads exhibiting definite changes, the severer the degree of coronary insufficiency.[54] It is pointless, and in fact undesirable, to take 12 lead electrocardiograms after exercise, since it is essential to take tracings periodically for many minutes following exercise, and Leads I and II, and precordial leads V^4, V^5 and V^6 usually exhibit the most striking changes (Fig. 5).

A good correlation obtains between abnormal S-T changes in the electrocardiogram exercise test and direct demonstration of abnormal coronary flow dynamics studied by direct measurement of coronary flow and oxygen utilization in man,[43] as well as by correlation with operative findings at coronary endarterectomy.[55]

Robb and Marks have shown clearly that the type and degree of ischemic S-T segment depression (the only truly positive criterion) after exercise reflects the severity of the coronary disease.[54] It should be stressed that significant S-T segment depression reflects widespread myocardial ischemia. The development of major T wave inversions, runs of ectopic beats replacing normal rhythm, and transient bundle branch block are less specific changes but nevertheless suggestive of coronary insufficiency (Fig. 6).

The anatomic studies of Blumgart[56, 57] have shown that in patients with organic angina pectoris multiple coronary closures are usually found at autopsy with diffuse myocardial involvement. It is not surprising therefore that after recovery from myocardial infarction nor-

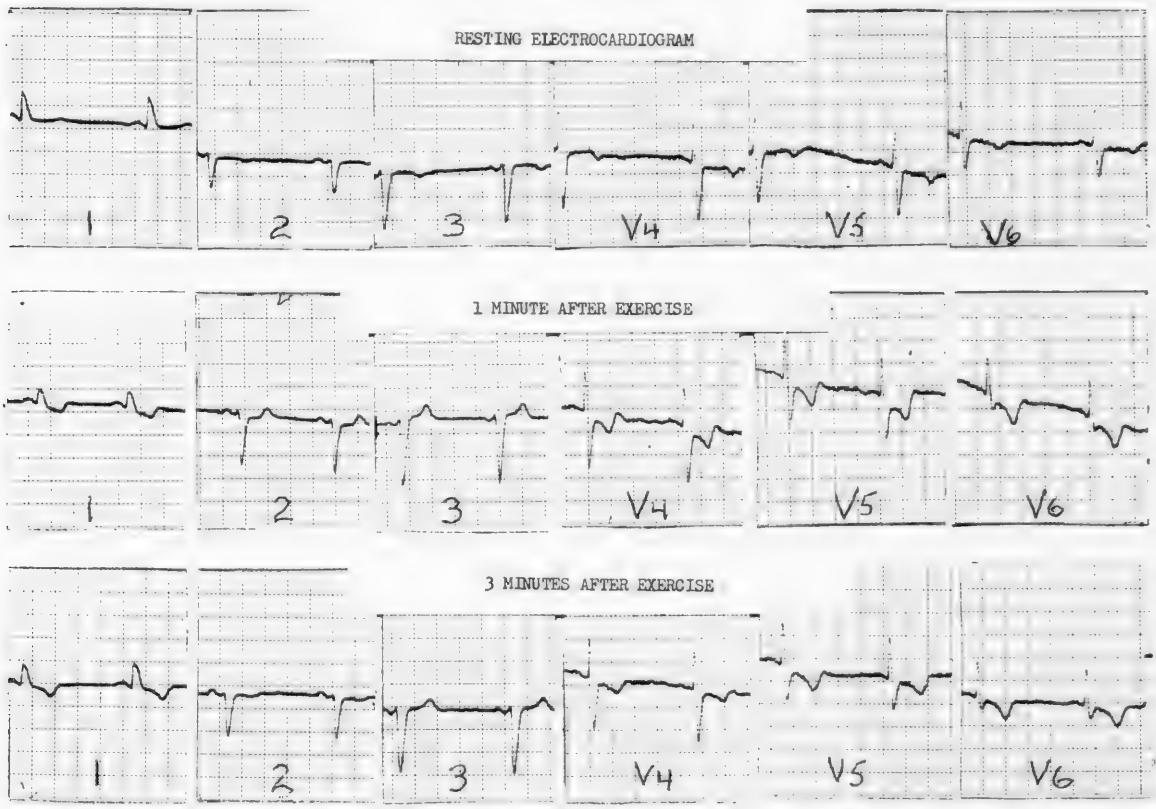


Fig. 7.—Functional evaluation with exercise test after myocardial infarction. The patient, a male building superintendent of 64, had suffered an attack of acute posterior wall infarction two months previously, with an uneventful recovery. After 30 ascents transitory slight pain developed and exercise was stopped. Tracings made immediately and three minutes after exercise reveal marked S-T depression and T abnormalities in Leads I, V_4, V_5, and V_6; and the T waves initially inverted in Leads II and III became upright in the immediate postexercise tracing. Such changes indicate severe residual ischemia following recovery from acute infarction. The patient died suddenly one month later. When the exercise test is normal after convalescence from an acute attack of infarction, as is commonly the case, earlier and more complete return to full physical activity may be encouraged.

mal exercise tests are often observed, for the ischemia in such instances may be localized to a confluent area particularly in persons who have suffered their initial attack. However, it is useful to perform exercise tests in evaluating ability to resume physical activity after an attack of myocardial infarction.[13] If no electrocardiographic signs of ischemia or pain develop with exercise, early and relatively full return to activity may be encouraged. Conversely, if decided evidence of ischemia appears (Fig. 7) caution is necessary in allowing resumption of an active life. This is an application of the exercise test which deserves more widespread employment.

Summary

The Master double two-step exercise test serves conveniently for the detection of coronary insufficiency, and for objective evaluation of chest pain, particularly since resting electrocardiograms are normal in approximately half of patients with angina pectoris. The test is useful also to detect latent coronary insufficiency in circumstances known to be attended by heightened incidence of coronary heart disease. These include hypercholesteremia and other serum lipid abnormalities, hypertension, obesity, diabetes, and arcus senilis. Since coronary heart disease is so widely prevalent and a prime cause of death, it appears desirable to employ the exercise test whenever cardiovascular surveys are conducted in adults, as in periodic health examinations. Another useful area of application is in the appraisal of functional recovery after convalescence from an attack of myocardial infarction.

A good correlation exists between abnormal S-T changes in the electrocardiogram exercise test and abnormal coronary flow dynamics studied by direct measurement of coronary flow and oxygen utilization in man. Postmortem studies on patients whose exercise tests had been abnormal regularly have shown severe generalized coronary artery narrowing. Death rates and subsequent attacks of myocardial infarction in those with positive tests are as high as 8 to 10 times that in persons with normal responses; hence abnormal findings have important prognostic significance.

The cause of S-T segmental depression in the electrocardiogram is not anoxia per se, but an abnormal potassium efflux from the myocardium provoked by ischemia. Electrocardiographic changes, and cardiac pain on performance of exercise, can be minimized or obviated by preloading patients with a potassium chloride infusion prior to the test. Conversely, depletion of myocardial potassium by prior intravenous infusion of sodium lactate greatly accentuates S-T abnormalities and pain on performance of exercise. The sodium lactate test may be employed as a substitute for the double two-step exercise test when exercise cannot be performed.

The dynamic factors responsible for cardiac pain in angina pectoris involve both myocardium and coronary arteries. In the myocardium potassium loss causes myocardial contracture and heightened potassium in the coronary veins causes venospasm. Heightened extracellular potassium, which is not washed away owing to impaired coronary flow, is responsible for protracted pain, arrhythmias, and sudden death in acute coronary artery occlusion. A dynamic factor in diseased coronary arteries contributing to the syndrome of angina pectoris is transitory total obstruction of coronary flow produced by a "flitter" effect, rather than coronary artery spasm. With an increased flow velocity, as occurs for example during tachycardia, lateral pressure is reduced and vessel walls are brought into apposition, transiently causing complete stoppage of flow. When the speed of flow is slowed by rest, carotid sinus pressure, or dilatation of the entire vascular bed by glyceryl trenitrate (nitroglycerin), "flitter" is terminated and flow is restored, with prompt abatement of pain as the accumulated potassium is washed away.

The factor of potassium loss from the myocardium bears importantly on the problem of false positive exercise tests. Where the myocardial potassium content is relatively low, as in older persons—particularly women—or persons with hypertension, myocardial disease, and heart failure, S-T changes are more readily induced by exercise. Similarly, food intake, insulin, anxiety with epinephrine release, tachycardia, and digitalis all lower myocardial potassium and favor the appearance of S-T segment changes on performance of exercise.

In general, the more marked the S-T depression and the longer these changes persist, the severer the degree of coronary insufficiency. The development of other abnormalities, such as major T wave inversions, significant arrhythmias and transient bundle branch block, are suggestive but less specific of coronary insufficiency than depression of the S-T segment. Leads I and II, and precordial leads V_4, V_5, and V_6 usually exhibit the most striking changes. These suffice for serial tracings which should be taken periodically for several minutes following exercise. Properly performed and interpreted, and with recognition of limitations as

to specificity, the double two-step exercise test is a most useful clinical index of the functional adequacy of the coronary circulation.

(The author's address is Equitable Life Assurance Society of the United States, 393 Seventh Ave., New York 1, N. Y.)

References

Part I

1. Burnett, C. J.: Pain and Pain Equivalents in Heart Disease, *Ann. Int. Med.* 10:1156, 1937.
2. Master, A. M., and Rosenfeld, I.: The Master "2 step" Electrocardiographic Test Brought Up to Date, *Tr. A. Life Ins. M. Dir.* 43:70, 1959.
3. Master, A. M.; Friedman, R.; and Dack, S.: The Electrocardiogram After Standard Exercise as a Functional Test of the Heart, *Am. Heart J.* 24:777, 1942.
4. Wood, F. C., and Wolferth, C. C.: Angina Pectoris: The Clinical and Electrocardiographic Phenomena of the Attack and Their Comparison with the Effects of Experimental Temporary Coronary Occlusion, *Arch. Int. Med.* 47:339, 1931.
5. (*a*) Scherf, D., and Goldhammer, S.: Zur Frühdiagnose der Angina pectoris mit Hilfe des Elektrokardiogramms *Ztschr. klin. Med.* 124:111, 1933. (*b*) Hausner, E., and Scherf, D.: Über Angina pectoris Probleme *Ztschr. klin. Med.* 126:166, 1933.
6. Missal, M. E.: Exercise Tests and the Electrocardiograph in the Study of Angina Pectoris, *Ann. Int. Med.* 11:2018, 1938.
7. Master, A. M., and Oppenheimer, E. T.: Simple Exercise Tolerance Test for Circulatory Efficiency with Standard Tables for Normal Individuals, *Am. J. M. Sc.* 177:223, 1929.
8. Gubner, R. S., and Ungerleider, H. E.: Survey of Electrocardiographic Practice in the United States, *Circulation* 14:947, 1956.
9. Dawber, T. R.; Moore, F. E.; and Mann, G. V.: Coronary Heart Disease in the Framingham Study, *Am. J. Pub. Health* 47:(Supp.) April, 1957.
10. Feinberg, G. L.; Schwartz, M.; and Mansfield, R. J.: Screening Program Among Key Personnel in Industry: Emphasis on Routine Master Two-Step Exercise Test, *New York J. Med.* 56:3162, 1956.
11. Franco, S. C.: Conference on Heart in Industry, *M. Sc.* 6:468, 1959.
12. Brody, A. J.: Master Two-Step Exercise Test in Clinically Unselected Patients, *J.A.M.A.* 171:1195, 1959.
13. Gubner, R. S., and Ungerleider, H. E.: Newer Aspects of Clinical Electrocardiography, *New York J. Med.* 48:2491, 1948.
14. Russek, H. I.: The Electrocardiographic Master Exercise Test in the Evaluation of Drug Therapy in Angina Pectoris, Seminar on the Electrocardiographic Exercise Test, Vermont Heart Association, Burlington, Sept. 20, 1959.
15. Hellerstein, H. K.: Significance of an Abnormal Exercise Test, Seminar on the Electrocardiographic Exercise Test, Vermont Heart Association, Burlington, Sept. 20, 1959.
16. Robb, G. P.; Marks, H. H.; and Mattingly, T. W.: Value of Double Standard Two-Step Exercise Test in Detection of Coronary Disease, *Tr. A. Life Ins. M. Dir.* 40:52, 1957.
17. Mattingly, T. M.: Criteria and Significance of a Two-Step Exercise Test as Determined by Clinical Evaluation of Patients on Long Time Follow-up, Pathology Studies of Coronary Arteries in Patients Dying After the Test and Studies in Normals, Seminar on the Electrocardiographic Exercise Test, Vermont Heart Association, Burlington, Sept. 20, 1959.
18. Robb, G. P.; Marks, H. H.; and Mattingly, T. W.: Stress Tests in the Detection of Coronary Disease, *Postgrad. Med.* 24:4, 1958.
19. Robb, G. P.: Value of the Electrocardiographic Master Exercise Test as Determined from a Follow-up of One-Thousand Consecutive Tests in Military Personnel and in Life Insurance Applicants, Seminar on the Electrocardiographic Exercise Test, Vermont Heart Association, Burlington, Sept. 20, 1959.
20. Gardberg, M., and Rosen, I. L.: Electrocardiogram of the Month, *Current M. Dig.* Sept., 1959, p. 75.
21. Horlick, L.: A Clinical Re-Evaluation of Master's Two-Step Test, *Canad. M. A. J.* 80:9, 1959.
22. (*a*) Master, A. M.; Field, L. E.; and Donoso, E.: Coronary Artery Disease and "Two-Step Exercise Test," *New York J. Med.* 57:1051, 1957. (*b*) Master, A. M.: The "Two-Step" Exercise Electrocardiogram: Its Use in Heart Disease, Including Valvular Heart Disease of Adults, *Bull. St. Francis Sanit.* 10:1, 1953.
23. (*a*) Master, A. M. and Rosenfeld, I.: The Master "2-Step" Electrocardiographic Tests Brought Up to Date, *Tr. A. Life Ins. M. Dir.* 43:70, 1959. (*b*) Rosenfeld, I.; Donoso, E.; and Master, A. M.: Interpretation of the Master "2-Step" Exercise Electrocardiogram by Quantitative Analysis of RS-T Segment, *Proc. Soc. Exper. Biol. & Med.* 103:320, 1960.
24. White, N. K.; Edwards, J. E., and Dry, T. J.: The Relationship of the Degree of Coronary Atherosclerosis with Age in Man, *Circulation* 1:645, 1950.
25. Scherf, D., and Schaffer, A. T.: Electrocardiographic Exercise Test, *Am. Heart J.* 43:927, 1952.

Part II

26. Gubner, R. S.: An Appraisal of the Exercise Electrocardiogram Test: Part I—Applications, Significance and Criticisms, *J. Occup. Med.*. 2:57, 1960.
27. Gubner, R. S., and Ungerleider, H. E.: Long Term Prognosis and Insurability in Coronary Heart Disease, *Am.. Heart J.* 58:436, 1959.
28. Gubner, R. S., and Ungerleider, H. E.: Electrocardiographic Criteria of Left Ventricular Hypertrophy: Factors Determining the Evolution of the Electrocardiographic Patterns in Hypertrophy and Bundle Branch Block, *Arch. Int. Med.* 72:196, 1943.
29. Wolferth, C. C.; Bellet, S.; Livezy, M. M.; and Murphy, F. D.: Negative Displacement of the RS-T Segment in the Electrocardiogram and Its Relationships to Positive Displacement; an Experimental Study, *Am. Heart J.* 29:220, 1945.
30. Hellerstein, H. H., and Katz, L. N.: The Electrical Effects of Injury at Various Myocardial Locations, *Am. Heart J.* 36:184, 1948.
31. Master, A. M.; Gubner, R. S.; Dack, S.; and Jaffe, H. L.: Differentiation of Acute Coronary Insufficiency with Myocardial Infarction from Coronary Occlusion, *Arch. Int. Med.* 67:647, 1941.
32. Gubner, R. S., and Behr, D. J.: Role of Electrolytes in Origin of Ischemic Cardiac Pain and Associated Electrocardiographic Abnormalities, *Circulation* 16:889, 1957.
33. Gubner, R. S., and Behr, D. J.: Effect of Sodium Lactate and Potassium Chloride on Electrocardiogram and Exercise Tolerance in Coronary Disease, *Clin. Res. Proc.* 5:163, 1957.
34. Kreuziger, H.; Asteroth, H.; and Zipf, K.: Kaliumveränderungen nach Herzinfarkt im Tierexperiment, *Ztschr. Kreislaufforsch.* 43:385, 1954.
35. Harris, A. S.; Bisteni, A.; Russell, R. A.; Brig-

ham, J. C.; and Firestone, J. E.: Excitatory Factors in Ventricular Tachycardia Resulting from Myocardial Ischemia—Potassium a Major Excitant, *Science* 119: 200, 1954.

36. Herles, F., and Daum, S.: Abnormalities of Electrolyte Distribution in the Myocardium with Myocardial Infarcts and Coronary Changes in the Electrocardiogram, *Cas. Lek. Ces.* 96:1050, 1957.

37. Jennings, R. B.; Crout, J. R.; and Smetters, G. W.: Studies on Distribution and Localization of Potassium in Early Myocardial Ischemic Injury, *A.M.A., Arch. Path.* 63:586, 1957.

38. Russell, R. A.; Crafoord, J.; and Harris, A. S.: Ventricular Myocardial Composition After Experimental Coronary Occlusion, *Fed. Proc.* 17:138, 1958.

39. Hajdu, S.: Mechanism of Staircase and Contracture in Ventricular Muscle, *Am. J. Physiol.* 174:371, 1953.

40. Levine, S. A.: Some Notes Concerning Angina Pectoris, *J.A.M.A.* 171:1838, 1959.

41. Rodbard, S., and Saiki, H.: Flow-Through Collapsible Tubes, *Am. Heart J.* 46:715, 1953.

42. Sones, M.: Personal communication to the author.

43. Gorlin, R.; Messer, J. V.; Levine, H. J.; Neill, W. A.; and Wagman, R. J.: Coronary Circulation in Health and Disease, *M. Clin. North America* 44:1181, 1960.

44. Laveque, P. E.: Atrial Arrhythmias and Myocardial Potassium, *Fed. Proc.* 17:388, 1958.

45. Gertler, M. M., et al.: Effect of Digitoxin and Quinidine on Intracellular Electrolytes of the Rabbit Heart, *Proc. Soc. Exper. Biol. & Med.* 92:629, 1956.

46. Conn, H. L., Jr., and Wood, J. C.: Acute Effect of Quinidine on Potassium Exchange and Distribution in the Dog Ventricle, *Am. J. Physiol.* 199:151, 1960.

47. Freedberg, A. S.; Riseman, J. E. F.; and Spiegel, E. D.: Objective Evidence of the Efficiency of Medicinal Therapy in Angina Pectoris, *Am. Heart J.* 22:494, 1941.

48. Anderson, E. C., and Laugham, W. H.: Average Potassium Content of the Human Body as a Function of Age, *Science* 130:713, 1959.

49. Ungerleider, H. E.; Duhigg, T. F.; and Gubner, R. S.: Examination of the Heart in Navy Applicants, *U. S. Naval M. Bull.* 41:441, 1943.

50. Holmgren, A.; Jonsson, B.; Levander, M.; Linderholm, H.; Sjöstrand; and Ström, G.: Electrocardiographic Changes in Vasoregulatory Asthenia and the Effect of Physical Training, *Acta med. scandinav.* 165: 259, 1959.

51. Wood, P.; McGregor, M.; Magidson, O.; and Whittaker, W.: The Effort Test in Angina Pectoris, *Brit. Heart J.* 12:363, 1950.

52. Mantero, O.; Longhini, E.; and Tossi, B.: De l'Importance diagnostique de l'épreuve de l'hypoxémie dans l'evaluation clinique de l'hypertrophie myocardique, *Arch. mal. coeur* 52:912, 1959.

53. Lepeschkin, E., and Surawicz, B.: Characteristics of True-Positive and False-Positive Results of Electrocardiograph Master Two-Step Exercise Tests, *New England J. Med.* 258:511, 1958.

54. Robb, G. P., and Marks, H. H.: Evaluation of Type and Degree of Change in Post-Exercise Electrocardiogram in Detecting Coronary Artery Disease, *Proc. Soc. Exper. Biol. & Med.* 103:450, 1960.

55. Kattus, A.; Longmire, W. P.; Cannon, J. A.; Winfield, M. E.; and Davis, J. H.: Diagnostic and Functional Evaluation of Candidates for Coronary Endarterectomy, *A.M.A. Arch. Int. Med.* 104:870, 1959.

56. Blumgart, H. L.; Schlesinger, M. J.; and Davis, D.: Studies on the Relation of the Clinical Manifestations of Angina Pectoris, Coronary Thrombosis, and Myocardial Infarction to the Pathologic Findings, *Am. Heart J.* 19:1, 1940.

57. Zoll, P. M.; Wessler, S.; and Blumgart, H. L.: Angina Pectoris: A Clinical and Pathologic Correlation, *Am. J. Med.* 11:351, 1951.

AMERICAN MEDICAL ASSOCIATION

will present

A SERIES OF REGIONAL MEDICOLEGAL CONFERENCES

One of these meetings will be held in San Francisco on March 10-11 at the Mark Hopkins Hotel; another, in Louisville, on April 14-15 at the Kentucky Hotel; and a third, in New York City on April 28-29 at the Statler Hilton Hotel.

Some of the subjects that will be covered are: Res Ipsa Loquitur in Medical Professional Liability Cases, the Use and Misuse of Demonstrative Evidence in Personal Injury Cases, Medical Expert Testimony and the Status of Medicolegal Relations. One half day will deal with a discussion of developments and trends in our judicial procedures. Included will be a consideration of the separation of the questions of liability and damages in the trial of a case, impartial medical testimony projects, developments in pre-trial hearings and discovery procedures and the "liability without fault" approach to all personal injury litigation. The final half day of the program will deal with a discussion of the most important cases in the medicolegal field during the past 18 months. Outstanding physicians and attorneys will be speakers.

The registration fee for each conference will be $5.00. This covers the cost of a luncheon on Saturday and any proceedings of the meeting that may be published. For further information, write: C. Joseph Stetler, Director, Legal and Socio-Economic Division, American Medical Association, 535 North Dearborn, Chicago 10, Illinois.

Physical Fitness and Motor Vehicle Accidents

Robert P. Sim, M.D., Pelham, N. Y., and Harold Brandaleone, M.D., New York, N. Y.

IT IS NOT necessary to reemphasize the impact of motor vehicle accidents on vital statistics in the United States. In a recent release, the World Health Organization pointed out that present-day man has nearly as good a chance of dying a violent death as of dying in his bed. In 1956, the United States annual death rate for "accidents, poisoning and violence" was 71.3 per 100,000. Of these, one-third were due to motor vehicle accidents. Many thousands of others are casualties without being killed. The impact on the economy of the country is terrific.

The IMA Committee on Standards for Motor Vehicle Drivers has published recommendations covering the selection of presumably safe commercial drivers by medical examination. By such means, men with gross defects may be eliminated, leaving a balance of drivers who are considered physically fit to drive. Nonetheless, accidents still occur. The IMA Committee further investigated by means of a small sample study in which drivers were matched, the variable being whether or not the individuals had had accidents. It turned out that the accident drivers had significantly more physical defects of record and that these fell in the musculoskeletal and neuropsychiatric systems. This appeared to be a positive finding until a statistical fallacy became apparent, i.e., the defect may have had nothing to do with the accident. A new study was designed to explore this possibility, the hope being that some aspect of objective physical examination would serve to flag the driver more likely to have an accident.

Presented at the Forty-Fourth Annual Meeting of the Industrial Medical Association, Chicago, Illinois, April 29, 1959.

Dr. Sim is Assistant Medical Director, Esso Standard Oil Company. Dr. Brandaleone is Assistant Clinical Professor of Medicine, New York University College of Medicine.

Method

Eleven industrial physicians were requested to report on drivers—men who were not selected but who appeared for regular periodic examinations during the second six months of 1958. Subsequently, information was secured on their accident records during the five years preceding the examination. The form used was simplified to encourage cooperation. It was

CONDITIONS PRESENT AT
ROUTINE EXAMINATION OF MALE DRIVER

IDENTIFICATION NO. ____ AGE ____ DRIVING EXP. ____ YRS. ____ DATE OF EXAM ____

FINDINGS	NORMAL	ABNORMAL	DESCRIPTION OF ABNORMALITY
1. C.N.S. AND PSYCHIATRIC			
2. VISION			
3. HEARING			
4. CARDIOVASCULAR			
5. GASTROINTESTINAL			
6. RENAL			
7. METABOLIC			
8. MUSCULO-SKELETAL			
9. DRUG HISTORY	NO	YES	
10. ALCOHOL HISTORY	NO	YES	

DIAGNOSIS (IF ANY) ____

IS MAN'S PRESENT HEALTH STATUS THE SAME ___ BETTER ___ OR WORSE ___
THAN IT WAS FIVE YEARS AGO?

GIVE DATES OF EACH PREVENTABLE OR
AVOIDABLE ACCIDENT IN PAST FIVE YEARS ____

Table I—Physical Fitness and Motor Vehicle Accidents

Distribution: Age						
Group	Age	Total Sample	Accident Group	Accidents Chargeable to Accident Group	Ratio Accident % to Accident Group %
A	25-39	(62) 32.2%	(27) 38.6%	(42) 34.4%	0.89
B	40-49	(76) 39.6%	(29) 41.4%	(57) 46.7%	1.13
C	50-64	(50) 26.0%	(13) 18.6%	(21) 17.2%	0.92
	Unspecified	(4) 2.2%	(1) 1.4%	(2) 1.7%	
	Totals	(192) 100.0%	(70) 100.0%	(122) 100.0%	

Table II—Physical Fitness and Motor Vehicle Accidents

Distribution: Driving Experience					
Group	Years Experience	Total Sample	Accident Group	Accidents Chargeable to Accident Group	Ratio Accident % to Accident Group %
A	5-9	(47) 24.5%	(21) 30.0%	(36) 29.5%	0.98
B	10-14	(76) 39.6%	(28) 40.0%	(53) 43.4%	1.08
C	15-19	(23) 11.9%	(6) 8.5%	(9) 7.4%	0.87
D	20+	(42) 21.8%	(12) 17.1%	(18) 14.7%	0.86
	Unspecified	(4) 2.2%	(3) 4.4%	(6) 5.0%	
	Totals	(192) 100.0%	(70) 100.0%	(122) 100.0%	

Table III—Physical Fitness and Motor Vehicle Accidents

Correlation of Physical Findings with Accident Experience and Age

Group	Driving Exp. 10-14 Years: Total Cases	% with Musculoskeletal Defects	Total Defects	Age 40-49 Years: Total Cases	% with Musculoskeletal Defects	Total Defects
No-accident	48	(10) 21%	(22) 46%	47	(13) 28%	(25) 53%
Accident	28	(6) 21%	(12) 43%	29	(9) 31%	(12) 41%

further requested that men reported upon have at least five years' driving experience, since it is recognized that the young in years and experience have proportionately more accidents.

Results

One hundred ninety-two questionnaires were received. The drivers were symmetrically distributed with regard to age and driving experience. All were found by the examining physicians to be physically fit to drive. In other words, men with grossly disqualifying defects had already been eliminated. During the five years preceding the study, 70 men, or 36%, had accidents. These 70 men had a total of 122 accidents which were judged to be avoidable by review committees in the respective companies.

Table I presents the age distribution of the whole sample and of the accident group with the percentage of the accidents attributable to the age groups. Of interest is the ratio column, which shows that men under 40 and over 50 enjoy a better record than those between 40 and 50.

Table II presents a similar analysis based on years of driving experience. It is obvious that men with 10 through 14 years of experience have the least good record in this table.

It now remains to correlate these findings with the reported physical defects, remembering that the defects did not cause the men to be disqualified from driving.

Table III presents the reported defects. The B groups from Tables I and II have the highest accident rates and were chosen for comparison. The presence of musculoskeletal defects, being at comparable rates, bears no relationship to accident experience in either of the test groups, nor do the total defects reported give clues of statistical significance. A similar comparison for neuropsychiatric defects could not be made, since all reported cases fell in the no-accident category.

Table IV shows that defects in the body systems have a slightly higher prevalence in the no-accident group, arriving at the total of 45%. Lest anyone think this figure is on the high side, Dr. Leo Wade has reported that 80% of employed persons aged 20 to 65 years have defects worthy of diagnosis. This is evidence that the present sample reflects selection by the examining doctors. Of some interest is the subjective evaluation by the examining doctors, who reported 16% of the no-accident people in worse condition than five years before versus 13% for the accident group.

Table IV also shows that 58% of the men in the whole sample were without defects. If the presence of defects has no bearing on accident occurrence, one would expect to find this same 58% in the accident group. Actually, 63% of these men have no defects of record and account for a closely similar percentage (62%) of the total accidents. This points out that those having accidents do so at comparable rates regardless of physical defects which, in the examining physician's opinion, are not disqualifying.

Table IV—Physical Fitness and Motor Vehicle Accidents

All Ages	Total No.	With Defects: No.	With Defects: %	% of Accidents	Without Defects: No.	Without Defects: %	% of Accidents
Sample	192	81	42	....	111	58	....
Accident	70	26	37	38	44	63	62
No-accident	122	55	45	....	67	55	....

Conclusions

1. In a group of men approved for commercial driving on the basis of absence of disqualifying physical defects, the accident rate is the same in those with no defects as in those with nondisqualifying physical defects.

2. The effort to find clues to accident avoidance by disassociated physical examination is not rewarding.

3. Age and driving experience do not help in arriving at criteria for selecting safe drivers.

4. A statistical study of this type cannot relate particular accidents to the presence or absence of physical defects which may or may not have had some bearing at the time of accident.

5. It is suggested that a prospective study be undertaken to correlate the facts pertaining to individual accidents immediately after their occurrence. Medical evaluation of the driver is but one aspect. Criteria of avoidability and of seriousness should be established. Only by the multidiscipline approach will clarification of causative factors pertaining to the driver be achieved.

(Dr. Sim's address is Hutchinson River Parkway, Pelham, N. Y.)

The Treatment of Industrial Hand Injuries

III. BONE AND JOINT INJURIES

Burton C. Kilbourne, M.D., and Eudell G. Paul, M.D., Chicago, Ill.

FRACTURES and dislocations of the metacarpals and phalanges are extremely common industrial injuries. They range in severity from the undisplaced transverse or longitudinal fracture of the tuft of the distal phalanx to the markedly comminuted, open, articular fracture of the proximal phalanx or metacarpal. In a review of 153 patients treated for injuries of hospital severity, multiplicity of fractures was common.[1] As contrasted to fractures of non-industrial origin, open fractures were six times as frequent as closed fractures. The phalanges of the index finger are the site of the greatest number of digital fractures; of the metacarpals, the fifth is most frequently injured. Dislocations occur more frequently in the proximal interphalangeal joint. One fourth of the fractures were accompanied by damage to an adjacent tendon. Injuries were so severe as to cause loss of the digit in one of eight fractures.

The forces producing fractures and dislocations include direct or transmitted contusion, torsion, and lateral and vertical compression. The contusion and torsion forces are less likely to produce associated wounds of the soft tissues, and comminution is less frequent. Severe compression or crushing forces result in the most extensive damage to the hand and its digits.

Examination includes inspection for swelling, discoloration, laceration, and deformity. The circulation should be evaluated. In serious crushing injuries, it is reassuring to observe good color and a prompt return of circulation after depressing the fingernail. In the absence of this response, one cannot be sure of the viability of the finger distal to the injury. A suspicion of fracture based on swelling and tenderness should be an indication for x-ray examination. Many undisplaced or incomplete fractures will be detected by this routine. One should apply cross strain to test the extended interphalangeal joints for lateral ligament ruptures which may occur with dislocations.

It is desirable to estimate the stability of the undisplaced shaft fracture from the clinical and x-ray examination. Evaluation of this characteristic in the displaced fracture may be possible only at operation or after closed reduction. In general, the oblique and comminuted shaft fractures are unstable, whether closed or open. Whereas a closed transverse fracture may be quite stable, a similar fracture with extensive soft tissue disruption may require internal splinting to prevent displacement. The effect of muscle tonus in producing angulation and overriding is very evident in fractures of the metacarpal bones and the proximal and middle phalanges. Except for displacement of dorsal and volar lip fractures of the base, these forces are not a factor in the terminal phalanx.

After careful evaluation by examination and x-ray we are ready to proceed with treatment. Early cleansing and closure of open wounds, and accurate reduction and immobilization of fractures, are mandatory. With correct evaluation of the problem, adequate facilities, and adequate assistance, every effort should be made to carry out an adequate definitive procedure. Joint stiffness and risk of infection are tremendously increased by delayed or secondary procedures. While some uncomplicated fractures can be treated without anesthesia, and some with procaine infiltration, a general anesthetic is required for treatment of complicated and multiple injuries.

When the fracture is stable, we prefer the use of simple curved splints and a pressure dressing.[2] Open reductions are avoided unless there is indication. We are always prepared for a more effective open method, however, if there is doubt as to the success of closed reduction or of a less involved method of fixation. In our experience, fine Kirschner transfixing or intra-

Dr. Kilbourne is Assistant Medical Director and Dr. Paul is a member of the Medical Department of the International Harvester Company.

Submitted for publication, Nov. 18, 1960.

medullary wires are frequently necessary.[3-6] In multiple fractures, this method may be combined with use of the universal hand splint.[7] Traction is effective in some instances. Small screws are occasionally ideal.[8] In all cases we strive to splint the hand and fingers in the *position of function*, recognizing that we may encounter unexpected joint stiffness. In some of the badly comminuted joint fractures, a primary arthrodesis, or digital recession is preferable to a futile attempt at joint restoration. Frequently a primary amputation is indicated.

Fractures of the Distal Phalanx

The transverse or comminuted fracture of the tuft and shaft of the distal phalanx usually presents no problem of displacement or instability. The closed injury is often accompanied by a painful subungual hematoma. Treatment consists in windowing the nail to evacuate the blood, and use of a small compression dressing and splint. The splint may be bandaged to the volar surface from the level of the middle phalanx, to allow flexion in the middle joint. Some patients prefer an aluminum cage splint for the protection afforded against further contusion at work. Warm soaks and exercise of the distal joint should be started in 10 days to 2 weeks. Then, the splint may be discarded except when the patient is working. Since bony union will not be observed by x-ray for many months, resolution of swelling and tenderness, and resumption of normal activity are the criteria for discharge from active treatment. In a few instances nonunion is observed even after a year. The fibrous union is usually so dense, however, that good painless function returns.

An open fracture at this site may be considerably displaced. After cleansing and debridement, the fragments are usually well stabilized by suturing the skin wounds.

The common dorsal lip fracture of the base of the distal phalanx resulting from "baseball" type injury must be treated by restoration of the tendon-attached fragment to its bed. If this is not possible and the fragment will interfere with distal joint action, removal of the fragment and re-attachment of the extensor tendon to the base of the distal phalanx are indicated. As described under treatment of tendon and nerve injuries in the previous article of this series,[10] the distal joint must be hyperextended and the middle joint flexed to attain maximum relaxation of the extensor mechanism. The fragment is pressed back into its position to be held by bandaging the finger. The problem of supporting the finger in this position has not been solved by use of the molded plaster cast in our experience. More positive splinting can be accomplished by use of an axial Kirschner wire drilled through the volar aspect of the distal phalanx, through the hyperextended distal joint into the middle phalanx (Fig. 1). The proximal interphalangeal joint is splinted in 60° flexion by an aluminum or plaster splint.[9] It seems desirable to limit the use of the wire to transfixion of the distal joint rather than to attempt to include stabilization of the proximal interphalangeal (middle) joint of the finger. If the latter is held in semiflexion by the aluminum splint, we believe there is less chance of subsequent pain and restriction of motion at this joint.

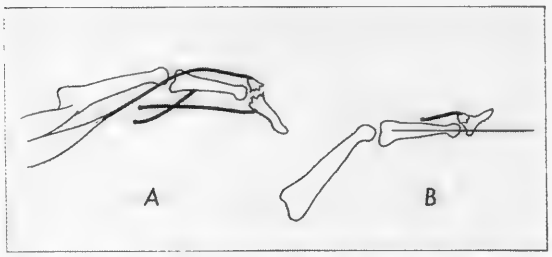


Fig. 1—A. The unapposed pull of the deep flexor tendon produces the typical "Mallet" deformity when the dorsal lip of the base of the distal phalanx is separated. B. To relax the extensor mechanism and allow repositioning of the fragment, the distal joint is pinned in hyperextension and the middle joint is splinted in semiflexion.

When an open fracture of this type is encountered, we prefer using a No. 34 stainless steel "pull-out" suture to overcome the tendon retraction and to stabilize the replaced fragment. Here again, hyperextension of the distal joint is maintained by Kirschner wire transfixion.

Fractures of the Middle Phalanx

Fractures of the middle phalanx may be transverse, oblique, or comminuted when the shaft of the phalanx is involved. The relationship of muscle pull to deformity is illustrated in Fig. 2*A*. Depending upon the degree of soft tissue disruption and the pattern of the fracture, there will be no displacement, or marked angulation or orverriding. The stable, transverse, or longitudinal shaft fracture can be treated adequately by supporting the finger in 55° flexion over a curved aluminum splint.

The usual deformity is volar buckling of the shaft fragment. A displaced transverse fracture at this site can be reduced over the curved aluminum splint, and redisplacement avoided by the pressure of the splint and relaxation of muscle pull.

Should the fracture be comminuted, pulp

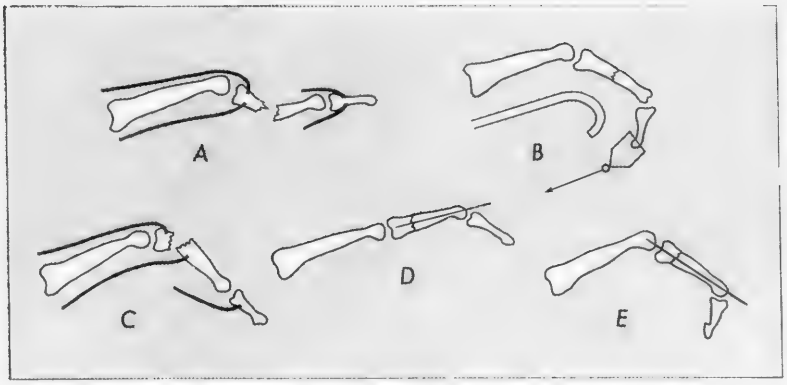


Fig. 2—A. Volar buckling of the fractured middle phalanx is observed when the lesion is distal to the insertion of the superficial flexor tendon slips. B. A curved volar splint may suffice to prevent angulation in a transverse fracture. If greater stability is needed, the traction safety pin here shown, or an intramedullary pin, is chosen. C. Dorsal buckling occurs when the fracture is proximal to the insertion of the superficial flexor tendon. D and E. Serial diagrams represent the use of an intramedullary pin and the final flexed position after stabilization is accomplished.

traction over the curved splint will be necessary to prevent the splaying of fragments caused by extensor and flexor muscle tonus. When dealing with an oblique displaced fracture, traction seems to be less effective than use of intramedullary or crisscross Kirschner wire fixation. Without positive accurate fixation, the oblique fractures tend to override or rotate to produce greater disability than occurs with comminuted fragments. With any method the finger should be splinted in functional semiflexion.

When dorsal buckling occurs, the fracture is usually near the base. This allows unapposed long extensor action to extend the proximal fragment. The distal fragment is brought into a position of extension to obtain reduction. Because of the shortening of the collateral ligaments and joint stiffness which occur when the finger is splinted in extension, we prefer to obtain reduction in extension, stabilize with transfixion wires, and then splint the digit in semiflexion. If a single axially placed Kirschner wire is used, the wire is started from the dorsal aspect of the semiflexed distal phalanx and advanced through the medullary canal of the distal fragment of the middle phalanx. The fracture is reduced and drilling continues until the proximal fragment is engaged. Then the middle joint is flexed to 45°–50°; the wire may be advanced across the joint into the head of the proximal phalanx. An alternative technique is to use two obliquely placed wires drilled in from the lateral aspects of the finger. In this manner sufficient stability may be obtained without passing through the joint to allow semiflexed splinting of the digit.

The question of producing stiffness by passing wires through joints may be raised. We prefer to avoid transfixing joints if possible, but in the fractures described above the disability from inaccurate immobilization is felt to be greater than that attributable to the wire passing through a joint. Another objection to wires is that of increasing the risk of infection when the wires are left projecting through the skin. With adequate skin preparation at a primary definitive procedure we have not encountered an infection attributable to this method. Secondary procedures during the first three weeks after an open injury are complicated frequently by wound infections. This fact emphasizes again the need for an adequate positive method originally.

Fractures of the Proximal Phalanx

The shaft and basal fractures of the proximal phalanx buckle volarward as a result of muscle tensions (Fig. 3*A*). Depending on the displacement and stability after reduction, we choose for immobilization a curved volar splint, traction, or intramedullary pinning. Although taping the finger over a bandage roll can be used satisfactorily in some instances,

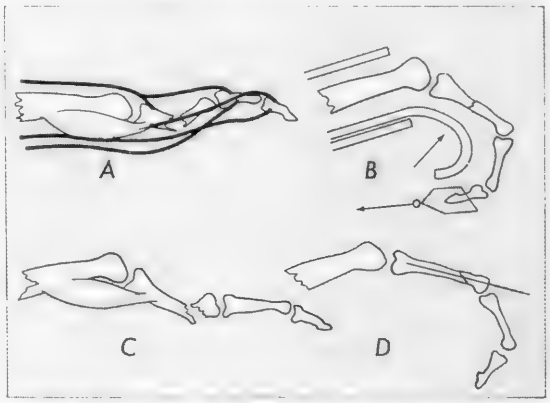


Fig. 3—A. Here is represented the deformity in fractures of the shaft of the proximal phalanx. Interosseus muscle pull angulates the proximal fragment volarward. B. Reduction is obtained over a curved volar splint. The finger may be taped to the splint to maintain position, or traction may be applied, as illustrated. C. The common deformity of a fracture through the neck of the proximal phalanx is shown. D. Because of the shortness of the distal fragment and obliquity, this reduction nearly always requires pin stabilization.

better relaxation of muscle pull and less chance for redisplacement are obtained by immobilizing the wrist, metacarpal, and involved finger. With the wrist in 40° dorsiflexion, a light cast is applied from the distal forearm to the palmar crease. After the first few layers of plaster have set, a precurved aluminum splint is superimposed upon the injured finger and palmar portion of the cast, using care that the fingertip will not be rotated. Additional layers of plaster are added. In its final position the splint and fingertip should be curved so that all joints are semiflexed, and the tip points to the navicular tubercle at the wrist. The finger is taped or bandaged evenly to the splint.

Again, should comminution be a problem, pulp traction may be added to maintain phalangeal length and better to stabilize alignment.

If there is an oblique, displaced fracture, one may prefer the intramedullary wire technique which is so necessary in fractures of this phalanx.

Fractures of the neck not only buckle anteriorly but the head of the phalanx may point dorsally at an angle of 90° (Fig. 3*C*). This distal fragment must be brought into line and held with an intramedullary pin directed proximally through the flexed middle joint (Fig. 3*D*).

In a closed reduction an immediate x-ray picture is needed to assure satisfactory position of fragments and pin. If an error is made, a small lateral incision can be made exposing the fracture. The distal fragment is rotated into the incision. The wire then can be drilled distally through this fragment until it is flush with the fracture margin. Reduction is accomplished. Retrograde (proximal) drilling introduces the sharpened butt end into the medullary canal under direct vision. The wire is cut ¼ inch distal to the skin surface, the skin incision closed, and the finger splinted in semiflexion. This principle of retrograde insertion of wires is frequently useful in other phalangeal and metacarpal fractures.

Fractures through the midshaft and neck of the proximal and middle phalanges will require three to five weeks' stabilization. Union of neck fractures requires greater time because of a circulatory factor; therefore we hesitate to remove the wires in less than four or five weeks. Fractures of the base of the proximal phalanx seem to acquire stability more quickly, because of better vascularity of this cancellous bone. One may often detect sufficient "stickiness" at this level to allow protected active motion and removal of the splint for "soaks" in 14 to 18 days.

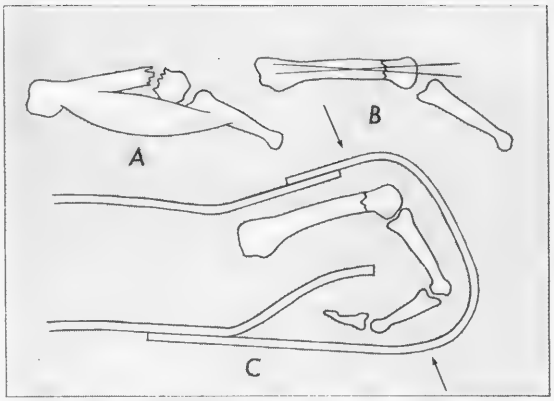


Fig. 4—A. Fracture through the neck of the metacarpal bone results in dorsal buckling and depression of the metacarpal head palmward. B. We prefer intramedullary pins inserted retrograde at open reduction unless the head is badly comminuted. In that event, finger traction over a curved splint is used. C. In principle, the forces applied here will reduce and hold this fracture. We use this method occasionally for a mildly depressed head, but avoid it where the volar pressure needed to hold reduction would risk necrosis of soft tissues under the proximal phalangeal head.

For fractures of the proximal phalanx of the thumb essentially the same rules of treatment apply. An exception should be noted when traction is applied. Here, an "outrider" of clothes hanger wire is incorporated in the cast. It extends in a curve toward the tip of the little finger, and should be long enough to allow room for the traction apparatus. Elastic bands under proper tension between the pulp traction "safety pin" and the "outrider" maintain alignment and counteract the muscle pull.

Fractures of the Metacarpals

The metacarpals will be considered collectively. The fracture through the neck results in volar angulation of the head of the metacarpal (Fig. 4*A*). If allowed to heal in this position, there is a painful prominence in the palm and function of the corresponding digit is limited. The fracture can be reduced by bringing the finger into acute flexion, then applying indirect pressure through the proximal phalanx. Dorsal counterpressure is applied proximal to the level of the fracture. Two methods of immobilization are available, as shown in Fig. 4*B* and 4*C*. We prefer the intramedullary pins for markedly depressed head fragments, and with open fractures. The pins are inserted more easily in the retrograde manner described for fractures of the neck of the proximal phalanx. Two wires are used in most instances, permitting better control over rotation. The corresponding

finger should be splinted comfortably in semiflexion, and a pressure dressing applied to the wound. Finger exercises are begun in two weeks and the wires are removed at four weeks.

We use the method depicted in Fig. 4*C* for fractures with mid volar angulation. One must provide a good sponge rubber pad beneath the head of the proximal phalanx to prevent pressure necrosis. A reasonable amount of pressure will be tolerated, but excessive pressure may produce a full-thickness slough of the dorsal skin over the proximal phalangeal head. The patient's complaint of a constant burning pain at this site should be considered an indication for prompt release of this pressure. We dislike keeping the finger in this position for more than two weeks. The creases macerate, and flexion contracture is a definite risk.

The shaft and basal fractures of these metacarpals vary greatly in severity. Many are open fractures with severe comminution. Most of the closed fractures present a transverse, oblique, or spiral pattern. All have the potentiality of angulation or rotation. Depending on associated tendon defects, there may be dorsal or volar buckling. In the spiral and oblique fractures, rotation with finger overlap on flexion is the rule.

To the choices of treatment outlined for the phalanges and the metacarpal head, we can add one more effective technique, i .e., the small bone transfixing screw.[8]

Again it seems logical to use the simplest effective method for the fracture (Fig. 5). In an undisplaced or incomplete fracture the hand cast with added aluminum finger splint holding the finger relaxed in semiflexion may be adequate. The fingers of the uninvolved metacarpal may be left free. In no instance, may the cast be applied to the hand alone without splinting the finger of the involved metacarpal.

If marked comminution is present, digital traction is applied with the pulp "safety pin" over the curved finger splint (Fig. 5*C*). The pull is exerted by rubber bands running from the "safety pin" traction device to a paper clip or other hook imbedded in the plaster cast volar to the navicular tubercle. This should be continued for three weeks.

In some instances of mild comminution or unstable transverse fractures, intramedullary and/or transfixing Kirschner wires may be applicable (Fig. 5*C*). These are usually left in for four weeks.

For the unstable oblique and spiral fracture we have been most pleased with the use of transfixion screws (Fig. 5*B*). These require

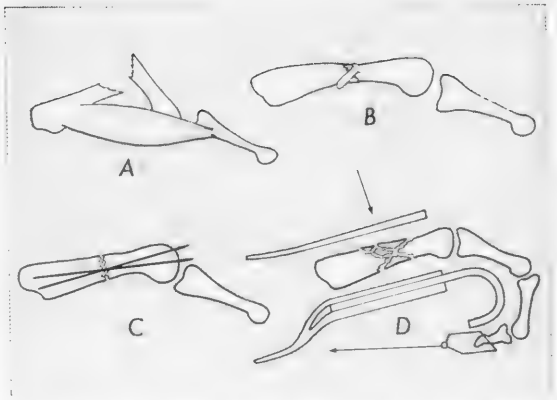


Fig. 5—A. Volar interosseus muscle tonus produces dorsal buckling of the fractured shaft of the metacarpal bone. B. When the fracture is oblique or spiral, a transfixation screw supplies positive apposition in anatomical position. C. For the transverse fracture, pins are frequently usefull. D. Traction is useful in the event of comminution of a metacarpal shaft.

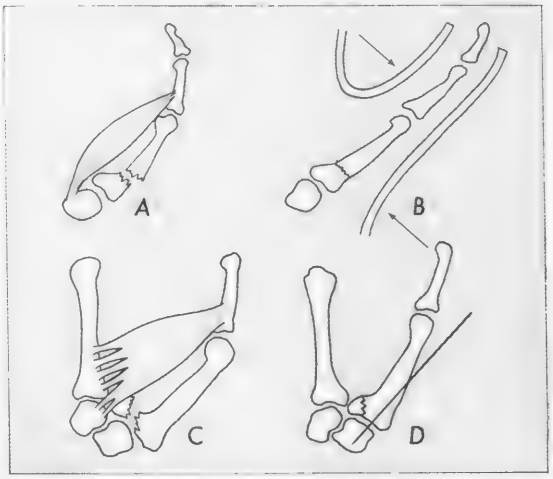


Fig. 6—In A and B are presented the deformity and the application of a molded cast for fracture of the first metacarpal. In C and D are shown a Bennett fracture and the prevention of redislocation by a transfixation pin.

an open reduction. As the fracture is held by a clamp in anatomical reduction, a No. 42 (0.093 inch) drill hole is made through the proximal cortex. A No. 47 (0.081 inch) drill is then used at the same angle through the deep cortex. The small screw is then inserted, drawing the fragments accurately together. Should the fracture be a long spiral, two screws may be used. The corresponding finger should be splinted for two to three weeks; then motion is allowed. Union will be solid in about six weeks.

Fractures of the first metacarpal occur usually in a transverse or comminuted pattern in

the shaft, tending to buckle dorsally (Fig. 6*B*). Closed reduction and a cast may be sufficient. The thumb is extended and pressure molding is maintained over the site of deformity as the plaster sets. Traction pins and the transfixing screw may be necessary as in the other metacarpals.

Bennett's fracture involving the hook process of the base of the first metacarpal results in a partial dislocation of the metacarpal from the greater multangular bone (Fig. 6*C*). If this subluxation is not corrected, a major disability ensues. The reduction may require operative exposure and accurate multiple pin transfixion. If possible, the hook process should be accurately reduced. Should it be small, the pins should stabilize the radial aspect of the base of the metacarpal to the greater multangular with full correction of the subluxation (Fig. 6*D*). When good correction is obtained, it will be best to prolong this fixation for five to six weeks to avoid subsequent slipping.

Dislocations

The proximal interphalangeal joint is most frequently the site of a dislocation. The metacarpal phalangeal, the distal interphalangeal, and the carpal-metacarpal joints are involved less often. When dislocation occurs, there is a capsular tear. The collateral ligaments may be disrupted. A marginal bone chip may be pulled off if the ligament withstands the strain. X-ray studies are therefore desirable. Reduction may have been accomplished by the patient or in the first-aid department. A quick pull without anesthesia may be successful in allowing the dislocated base of a phalanx to ride back in place.

If the joint then seems stable, we assume that only the capsule has been torn. If lateral instability is present, the collateral ligaments are torn or a marginal chip is avulsed. These digits should be immobilized for three weeks to allow healing of the capsule and ligaments and subsidence of synovitis. Earlier motion is prone to intensify synovitis and result in a chronically swollen and painful joint.

Operative intervention is required when the head of the 1st metacarpal bone becomes caught between the two tendinous insertions of the flexor brevis. When the interphalangeal joints are too unstable after reduction to be held by a splint, it would seem wise to carry out an early repair of the ligaments. In addition, transfixion pins may be used to assure protection of this delicate repair. Multiple pins are particularly useful in stabilizing the carpometacarpal joints.

Fractures and Severed Tendons

The primary treatment in these injuries should be that of the fracture. These are usually open wounds. A careful debridement is done, the fracture is stabilized, and healing is obtained before the tendon repair is considered. For secondary tendon repair and grafting technique, our previous section on tendons and nerves is cited. [10]

Summary

1. Undisplaced fractures of the phalanges and metacarpals should be treated simply. All fractures should be splinted in the position of function and motion instituted in two weeks if good stability is evident.

2. Open fractures are to be cleansed, debrided, and closed immediately to prevent infection. Primary definitive fracture treatment including pins and screws can be used to advantage when indicated in open fractures.

3. For unstable fractures, positive internal splinting by pins and screws is preferred to traction except when comminution leaves no choice.

4. Dislocated joints should be reduced and immobilized early and kept at rest for three weeks to allow healing of torn capsule and ligaments.

References

1. Kilbourne, B. C., and Paul, E. G.: Do's and Don'ts in the Treatment of Hand Injuries, *S. Clin. North America* 38:139-154 (Feb.), 1958.

2. Burnham, P. J.: Physiological Treatment for Fractures of the Metacarpals and Phalanges, *J.A.M.A.* 169: 663-666 (Feb. 14), 1959.

3. Berkman, E. F., and Miles, G. H.: Internal Fixation of Metacarpal Fractures Exclusive of the Thumb, *J. Bone & Joint Surg.* 25:816 (Oct.), 1943.

4. vom Saal, F. H.: Intramedullary Fixation in Fractures of the Hand and Fingers, *J. Bone & Joint Surg.* 35-A:5 (Jan.), 1953.

5. Cordrey, L. J.: Intramedullary "Pull-Out" Wire Fixation in Surgery of the Hand, *A.M.A. Arch. Surg.* 75:979-984 (Dec.), 1957.

6. Zelenock, M. N.; Larsen, R. D., and Posch, J. L.: Treatment of Fractures of the Hand, *A.M.A. Arch.* Surg. 75:320-338 (Sept.), 1957.

7. Allen, H. S., and Mason, M. L.: A Universal Splint for Immobilization of the Hand in the Position of Function, *Quart. Bull. Northwestern Univ. M. School* 21: 218-237, 1947.

8. Kilbourne, B. C., and Paul, E. G.: The Use of Small Bone Screws in the Treatment of Metacarpal, Metatarsal, and Phalangeal Fractures, *J. Bone & Joint Surg.* 40-A:375-383 (April), 1958.

9. Casscells, S. W., and Strange, T. B.: Intramedullary Wire Fixation of Mailet Finger, *J. Bone & Joint Surg.* 39-A:521-526 (June), 1957.

10. Kilbourne, B. C., and Paul, E. G.: The Treatment of Industrial Hand Injuries: II. Tendon and Nerve Injuries, *J. Occup. Med.* 2:549-553 (Nov.), 1960.

Organic Phosphate Insecticide Poisoning

David H. Reeder, M.D., Whittier, Calif.

SINCE the advent of the use of organic phosphate insecticides in agriculture there have been numerous cases of poisoning. Physicians who practice in rural communities are well aware of the problem, and a great deal of work is being done on the management of the chemical and the treatment of phosphate ester poisoning.

It has been fairly well established that the organic phosphate insecticides inactivate acetylcholinesterase in man as well as in experimental animals, so that acetylcholine accumulates at the parasympathetic postganglionic and sympathetic preganglionic synapses, as well as at the motor end-plates in striated muscle. Thus atropine, the ideal antagonist, is used to block the effect of the accumulated acetylcholine on the effector cell.

Symptoms usually begin with a dull headache, anorexia, muscular weakness, blurred vision, and fatigue. Dizziness and nausea soon follow, with abdominal cramps, vomiting, diarrhea, and feeling of constriction of the throat and chest with effort required to breath. Profuse sweating is usual. Difficulty in focusing vision may be present. Mental confusion becomes evident and twitching of the voluntary muscles may follow. Excessive salivation and lacrimation are frequent. Coma, collapse, pulmonary edema, and death after convulsive seizures are the usual route of demise.

The two patients whose cases are presented here acquired their poisoning in a plant where the chemical is added to agricultural dusting powders. The specific poison involved was tetraethylpyrophosphate, commonly known as TEPP. The men were clothed and wore respirators adequate to protect them in ordinary runs at the mixing mill. They started work at 8 a.m. At 9:30 a.m. the TEPP was added to the mix. Through an error, about 10 times the proper amount of TEPP was added, and the mix became gummy. This clogged the mill, and it was shut down. Both men had to climb into the mill to clean out the thickened mix. Both men had a lunch hour at noon and returned to work at 1 p.m.

About 3 p.m., both men reported to their foreman that they were feeling nauseated, weak, and dizzy. Both were immediately presumed to have been poisoned by TEPP. Emergency measures were instituted which consisted of stripping off all clothing and washing the body thoroughly in running, fresh water. Both men were given 2 mg (3/100 grain) of atropine by mouth and immediately were transported to the emergency unit of our local hospital.

The safety engineer who reviewed the incident concluded that TEPP had been absorbed through the skin as a result of prolonged contact between perspiration-soaked clothing and the product mixture which had an unusually high content of the poison.

CASE 1—A 23-year-old man was admitted to the emergency room at the hospital at 4 p.m. on Oct. 12, 1956. He stated that he felt weak and slightly dizzy. Physical examination revealed a pulse rate of 88 with regular sinus rhythm. Respiration was at the rate of 28 per minute, regular and not labored. The pupils were pinpoint and did not react to light or in accommodation. The lungs were clear. The deep tendon reflexes were sluggish but equal. The blood pressure was 120/80 mm Hg in the right arm, and it remained close to this level throughout his course. Prior to the further administration of atropine, blood was withdrawn and sent to the laboratory for a cholinesterase determination.

The patient was put to bed at complete rest and on a clear liquid diet. He was given 1.2 mg of atropine intravenously every hour from 4 p.m. until 11 p.m. At 5 p.m. his condition was unchanged from that on admission. His pupils were still pinpoint. At 6:15 his pupils were still pinpoint and he had no new symptoms. At 8:15 his pupils were 4 to 5 mm in diameter. The patient still had no complaints except that he felt sleepy. The serum cholinesterase level was reported from the laboratory as 0.308 unit. (The cholinesterase determinations were all performed on plasma. A pH meter was used for the determination and figures used express pH change $|\Delta ph|$ per hour. Normals in this laboratory range from 0.25 to 1.36 ΔpH per hour.) The next day, at 12:15 a.m., the patient's pupils were 8 mm in diameter and were slightly irregular. The pupils were now reacting to light but not in accommodation. The patient was slightly disoriented and complained that his legs felt numb. Atropine was reduced to 0.6 mg every two hours. At 6:40 a.m. his pupils were of normal size and reacted to light and in accommodation. His respirations were normal. The atropine was discontinued.

At 9 a.m. his condition was still good but the nurses reported that he was slightly disoriented as to place and time. At 2:45 p.m. he was definitely confused, especially when he started to fall asleep, and he would arouse from sleep fighting. His dis-

Submitted for publication May 29, 1959.

Dr. Reeder is with the Standard Oil (California) Spray Chemicals Corporation.

turbance was sufficient to necessitate restraints. He was given 0.4 mg of atropine. On Oct. 14, at 9 a.m., the patient appeared normal and was placed on a soft diet. His course the next 24 hours was uneventful. His disorientation and confusion had cleared and he was discharged on Oct. 15. When he was rechecked one month later, cholinesterase was 0.75 unit. There were no abnormal findings, and the patient was discharged as fully recovered.

CASE 2—The second patient, a 42-year-old white man, had a history of some alcoholism. He had also received 2 mg (3/100 grain) of atropine by mouth at the plant. On admission he complained of some respiratory distress, a feeling of weight on the chest, and an inability to get a deep breath. Pupils were pinpoint. There were slight moist rales throughout his chest. His deep tendon reflexes were diminished bilaterally. The pulse was regular at a rate of 80 per minute. His blood pressure was 110/74 mm. Hg and remained at about this level throughout his hospital stay. Blood was drawn for a cholinesterase determination, and he was given 1.3 mg (1/50 grain) of atropine intravenously on admission and hourly after that.

At 5 p.m. he appeared to be about the same; his breathing was easier when given oxygen by nasal catheter. At 6:15 his pupils were 2 to 3 mm in diameter and his respiratory distress was completely relieved. Auscultation at this time revealed an occasional rhonchus in the chest, and the patient had developed a slight cough. His cholinesterase level was reported at 0.525 ΔpH per hour. The next day, at 12:15 a.m. his pupils were 8 mm in diameter and reacted to light and in accommodation. He complained of minimal respiratory distress described as weight and heaviness. By this time, however, his chest was clear to auscultation. At 6:40 a.m. he was disoriented, was having some delusions of mistreatment, and had to be restrained. Atropine was discontinued.

At 9 a.m. he was still disoriented. His chest was clear to auscultation. Respirations were easy. At 2:45 p.m. his disorientation and delusions had cleared. On Oct. 14, at 2:10 a.m., the nurse reported that the patient was restless. He was given 0.5 gm of phenobarbital sodium (¾ grain) by mouth, which had little effect. At 9 a.m. he had a slight cough and his general condition was good. He was ambulant and was placed on a soft diet. On Oct. 15, he was doing well and was discharged to his home on a soft diet. Rechecked one month later, the patient had recovered his usual state of health and was considered completely recovered. The cholinesterase level was 0.84 ΔpH per hour.

✦ ✦ ✦

A history of exposure to a phosphate ester in conjunction with the symptoms described would lead one to suspect poisoning by this agent. Confidence in the diagnosis is strengthened by a laboratory finding of lowered blood cholinesterase level. But one cannot wait for the results, as the patient requires immediate treatment. The two to three hours that it takes for the laboratory to run the test are critical hours in the care of the patient, and his recovery or death may be determined in this time. Regular cholinesterase determination on a group of employees in a local plant where these poisons are handled all the time has shown that plasma cholinesterase levels vary from 0.65 to 1.25 ΔpH per hour and red cell cholinesterase levels from 0.72 to 0.99 ΔpH per hour. (The same laboratory and techniques were used in determining these levels.) Just where the critical level falls is not positive. Those who work with this problem, however, believe that if the cholinesterase level falls below 0.50 ΔpH per hour there is danger to the employee and he should be taken out of the environment until his cholinesterase returns to its normal level.

One must accustom one's self to the use of heroic doses of atropine in the treatment of this poisoning. Varying amounts have been recommended, but it seems the consensus that 2 to 4 mg intravenously should be repeated at 5- to 10-minute intervals, until the patient is fully atropinized. Then he should be given enough to maintain him in that situation for about 48 hours.

(The author's address is 124 E. Hadley St., Whittier, Calif.)

SEVENTH CORNELL CONFERENCE ON INDUSTRIAL MENTAL HEALTH

will be held

May 15 and 16, 1961

This is the seventh conference to be held on the campus of Cornell University, Ithaca, N. Y., on various aspects of industrial mental health. These conferences are planned as an opportunity for industrial physicians and personnel workers to get together to discuss their mutual concern about the maintenance of mental health in industry. The topic this year will be "The Effective Use of the Psychiatrist by Industry: the Problems Which Are Within and Those Which Are Outside His Scope." For further information, contact Temple Burling, M.D., Conference Chairman, New York State School of Industrial and Labor Relations, The State University of New York, Cornell University, Ithaca, N. Y.

Industrial Medical Association

THE PRESIDENT'S MESSAGE

ROBERT E. ECKARDT, M.D.

ON APRIL 11, 12, and 13, in Los Angeles, the IMA will hold its 46th annual meeting. Several innovations will be introduced by our organization this year. Perhaps the most exciting of these will be the Intensive Refresher Courses and the Clinics in Trauma.

The Intensive Refresher Courses, limited to 40 members, will cover the following subjects: (1) Cardiology in Industry and (2) Treatment of Radiation Injury, given on Tuesday; and (3) Dermatology in Industry and (4) Hearing Conservation in Industry, given on Wednesday. Since each course will be given twice, an individual theoretically could attend all four courses. However, since attendance is limited in number, it may not be possible to accommodate all people in all courses. Hence send your letters of application early to IMA Headquarters, 28 E. Jackson Blvd., Chicago 4, Ill.

The Clinics in Trauma will be held on Tuesday morning from 8:30-10:00 and will be limited to 50 participants. The subjects to be covered are (1) Fractures and Crush Injuries of the Forearm and Hand, (2) Problems of the Back, and (3) Injuries of the Leg and Ankle. The Clinics are under the supervision of our Committee on Surgery. These two educational efforts of our Association are very exciting. It is my hope that the response to them wil be so enthusiastic that we can plan them as a part of each year's sessions. I hope your applications have already been received at Headquarters office.

The next innovation will be that all Association business, including the presentation of all awards, is scheduled to take place at our annual business meeting on Wednesday afternoon, leaving Wednesday evening free for our banquet to be a truly pleasant social evening of eating, dancing, and renewing acquaintances with old friends (and new ones, too) and their wives. Award winners, new officers and Board members, and selected VIP's will be introduced to our assembled banqueteers, but there will be *no speeches*. In fact there won't even be a *speakers' table*.

The remainder of our program looks just as exciting as the Intensive Refresher Courses and Clinics in Trauma. It begins on Tuesday morning with a panel on the Rehabilitation of the Industrially Injured, will have "Red" Johnstone as our C. O. Sappington Memorial Lecturer, and will continue Tuesday afternoon with a joint session with the AAIN. The Wednesday morning session will be devoted to The Chest and Industry and to Resuscitation Techniques.

Thursday we have two concurrent sessions going all day. Two topics, Aching Feet and Mental Health, will share the morning spotlight with Toxicology and Industrial Hygiene. Since AIHA is not with us, we shall have our own toxicological and industrial hygiene sessions at a practical clinical level. In the afternoon, as well as for two hours in the morning, general sessions on surgical and medical topics will be presented.

An interesting group of technical and scientific exhibits have been planned, and I am sure Bill Burns and our Scientific Exhibit Committee will make this an interesting and educational portion of our meeting, as usual.

Ladies' entertainment will include a hospitality room for coffee and informal meetings, as well as visits to Chinatown, Farmers Market, Olvera Street, Knott's Berry Farm and Marineland of the Pacific. A visit to Disneyland is scheduled for Friday so "Pop" can go along too. Believe me Disneyland is fun! I went there once with Carey McCord and Rex Wilson. You should have seen us on the rides!

Finally don't forget Hawaii!! Our Post-Convention Hawaiian Conference is another innovation. It was designed for you! Modest work, plus relaxation in the beautiful surroundings of Hawaii! How can you resist? Sign up now.

The attractions of our Los Angeles meeting will be too great for anyone to resist and too good for anyone to miss! Sign up NOW! I hope to see each and every member in Los Angeles. The advance program indicates this will be our greatest meeting. Your attendance in Los Angeles will assure that it is. Remember the dates—April 11, 12, and 13, 1961—in Los Angeles.

Book Reviews

RADIATION HYGIENE HANDBOOK. Hanson Blatz. Ed. 1. Price, $27.50. Pp. 927, with 272 illustrations. McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York, N. Y., 1959.

By THOMAS S. ELY, M.D.

This is a "handbook" in the best classical sense. Its thickness is a substantial fraction of its width, it has a soft cover, and it treats a tremendous breadth of material—from four-place logarithms to the lowest temperature ever recorded in Winnemucca, Nev. It will find much more use as a reference work than as something with which to curl up on a Sunday afternoon.

The style is more that of Marks' "Mechanical Engineers' Handbook" than Behrens' "Atomic Medicine," since the book was written primarily for the health physicist, industrial hygienist, and sanitary engineer. There are, however, sections and parts of primary interest to the physician. The Handbook will be of interest to the medical man in a radiation industry, but should be an important part of the library of the industrial physician whose responsibility extends beyond the strictly medical.

Sections containing basic tables provide information on meteorology, radioactivity of minerals, shielding characteristics, particle characteristics, and radioisotopes. A glossary is included to facilitate unambiguous interpretation and communication. Other sections could be grouped under the general headings of sources of radiation, detection and measurement of radiation, handling of radioactive materials, interaction of radiation with matter, biological effects of radiation, and radiation protection.

The section on Exposure Standards and Radiation Protection Regulations covers issuances of the National Committee on Radiation Protection and Measurement, American Standards Association, Atomic Engery Commission, and several other federal, state, and nongovernment sources. Many of the more useful standards and regulations are actually reprinted in the *Handbook*. The sections on radiation sources, in addition to treating industrial sources, provide data on the natural radiation we are all receiving, thereby helping to put other doses in a meaningful relationship; information on medical x-ray doses and reduction thereof may help to prevent the sometimes embarrassing but frequent position of having the largest portion of the dose to radiation workers come from the plant medical department. Medical personnel have a primary interest, if secondary responsibility, in the subject of radiation measurement, whether by ionization, scintillation, photographic, chemical, or solid-state methods. The sections on physiological effects, radiation protection, and skin decontamination are, of course, of direct interest to the physician.

The *Handbook*, a 927-page book on the subject of radiation hygiene, merely outlines the high spots in most cases, illustrating strikingly how large the field has become. Most sections contain useful reference lists for those who need to explore a particular subject further. The book has some 38 contributors —outstanding people in the many specialties involved in radiation hygiene. The last section was written by physicians primarily for physicians. It includes parts on selection of personnel, medical control of exposed workers, medical records, and medicolegal considerations. It is interesting to note that a physician has the last word.

Dr. Ely is Chief, Health Protection Branch, Office of Health and Safety, U.S. Atomic Energy Commission, Washington, D.C.

MEDICAL DEPARTMENT, UNITED STATES ARMY, PREVENTIVE MEDICINE IN WORLD WAR II: Vol. II. Environmental Hygiene. Editor in Chief Col. John Boyd Coates Jr., MC. for Preventive Medicine Ebbe Curtis Hoff, Ph.D., M.D. Price, $3.50. Pp. 404. Office of the Surgeon General, Department of the Army, Washington, D.C., 1955. For sale by the Superintendent of Documents, United States Government Printing Office, Washington 25, D.C.

By C. L. WILBAR JR., M.D.

The management by the Medical Department of the United States Army of environmental and sanitation factors concerned with the health of large numbers of military personal of this country engaged in an exceptionally mobile and mechanized global war makes a fascinating part of the history of World War II. This volume on Environmental Hygiene is one portion of the professional, clinical, and technical series concerning the history of the Medical Department. There is also an administrative and operational series.

Dr. Wilbar is Secretary of Health, Commonwealth of Pennsylvania, Harrisburg, Pa.

Each chapter is authored by one or two individual authors, but Col. Tom F. Whayne, M.C., formerly Chief of the Preventive Medicine Division of the Office of the Surgeon General, and Col. William A. Hardenbergh, Sn.C., formerly Chief of the Sanitary Engineering Division of the Office of the Surgeon General, together have written over half of this volume.

Besides the subjects anticipated by the reviewer of food sanitation, housing, water purification, waste disposal, and insect and rodent control, the last two chapters cover foreign quarantine and "Preventive Medicine in Ports of Embarkation and for Persons in Transit."

Since this was a type of war entirely different from what this country had ever before experienced and since much had been learned (or partially learned) about improved sanitation, immunization and other preventive medicine practices between the two world wars, much change and ingenuity were required for effectuating modern public health control measures. This volume brings out the many difficulties encountered—insufficient materials, breaking of old habits, using antiquated equipment for economy purposes, unusually rapid mobility of manpower, and dispute regarding where responsibility lay (particularly among the Medical Corps, Quartermaster Corps, Engineering Corps, and, in the case of foreign quarantine, other units of the federal government).

Interesting historical development of methods of handling the problem is included at the beginning of each chapter. This historical sequence varies in individual chapters as to length, form, and span of years covered, some going back into biblical times and other starting a few years before World War II.

The war and military organization provided a research opportunity in connection with testing new immunization procedures, new preventive durgs (such an antimalarials) and new chemicals to repel or kill insects and rodents. The chapter on research concerning insect and rodent control is fascinating when one realizes the far-reaching significance of the results of this research, done sometimes in cooperation with other agencies such as the Bureau of Entomology of the Department of Agriculture. A large portion of this all-too-short chapter on research deals with the problems concerned with the development of DDT, a "wonder" chemical of the war, if any can be called such. Anyone familiar with the history during World War I of the constant fight against lice by many of our troops overseas will be truly grateful for the statment made in one sentence in this chapter: "It was shown that mass delousing of troops could be effected by blowing or dusting DDT powder in pyrophyllite under the clothing, using a hand-operated dust gun."

The excellent progress in controlling the enemies to health in the environment of our military personnel in spite of tremendous obstacles at times, as is clearly and in some detail portrayed in this volume, unquestionably was largely responsible for the remarkable conquest of illness, mainly through prevention, which occurred in World War II. This was the first major war in which "natural" illnesses did not kill more military persons than battle casualties. Considering the teaching programs, described in this book, to millions of military personnel and concentrated education for health personnel, the results have undoubtedly carried over into civilian living since the war.

Publications Available

The following list of publications has been compiled on the basis of probable interest to the readers of this journal and is presented solely for the purpose of giving notice of their availability.

Hearing Loss. What Can Be Done About It. Greydon C. Boyd, M.D. Price, $1.45. Pp. 190, paperback. J. B. Lippincott Company, East Washington Square, Philadelphia 5, Pa.

The subject matter is presented for nonmedical readers. The structure and function of the ear are illustrated with line drawings. Consideration is given to types of hearing loss, their diagnoses, and therapy or rehabilitation. The substantive material of such things as pitch, intensity, decibel, audiometry, and hearing aid are presented in nontechnical fashion. An appendix lists the hearing rehabilitation centers of the country as of the date of publication (1959). There is a seven-page index.

Strike Back at Arthritis. Public Health Service Publication No. 747, 1960. Pp. 45, with illustrative drawings. Single copies available without charge from the U.S. Department of Health, Education, and Welfare, Public Health Service, Division of Occupational Health, Washington 25, D.C. Price $0.40 when ordered from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C.

This booklet describes therapeutic procedures that can be carried out in the home by the patient and his family. Designed to aid physicians in prescribing treatment for their arthritis patients and instructing them in proper care, the manual gives step-by-step instructions for 15 exercises which preserve or improve the range of motion of the involved joints. Two versions of each exercise are presented; one is for the patient who can perform independently, the other for the patient who needs assistance. Other sections deal with the importance of good posture, the use of heat, splinting, canes and crutches, and self-help devices.

Diabetes Program Guide. Public Health Service Publication No. 506, Revised 1960. Pp. 68. Single copies available without charge from the U.S. Department of Health, Education, and Welfare, Public Health Service, Division of Occupational Health, Washington 25, D.C. Price $0.50 when ordered from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C.

This booklet deals with the major elements of a

diabetes program, beginning with community resources and proceeding through primary and secondary prevention to finding and serving the diabetic patient. It covers such topics as physiology of the disease; types of screening projects for diabetes detection; diagnostic standards, tests, and laboratory procedures; and professional and community education. This revised edition includes final results of the diabetes test validation studies and reflects in various text changes newer thinking in diabetes management and detection.

Hazardous Substances Labeling Act: New Safety Labeling Requirements with Explanation and Committee Reports. Food-Drug-Cosmetic Law Reports. Extra Edition No. 273, July 13, 1960. Price, $1.00 (1-4 copies), $0.90 (5-9 copies), $0.85 (10-24 copies), $0.75 (25-49 copies), $0.70 (50-99 copies). Pp. 31. Commerce Clearing House Products Co., 4025 W. Peterson Ave., Chicago 46, Ill.

This booklet, prepared by Commerce Clearing House, Inc., discusses the Federal Hazardous Substances Labeling Act, enacted into law by congress on July 12, 1960. The text covers the purpose of the Act, a summary of its provisions, the definitions of hazardous substances, various household products which may contain hazardous substances, exempt substances, and requirements for label statements. The full text of the law and pertinent congressional committee reports are included.

Questions

The questions published in this column are edited versions of requests for information that have been received during recent months. The answers have been prepared by one or more competent authorities in the particular area covered by the question. Readers may address questions to the Editor.

QUESTION: *What are the indications for surgical removal of foreign bodies, giving consideration to various substances in different locations?*

ANSWER: Without exception, nonmetallic foreign bodies such as wood, plastics, dust, clothing, dirt, grease, oil, and the like should all be removed promptly, since, in contradistinction to metallic and glass foreign bodies, these organic materials will cause local tissue reaction, cellulitis, and lymphangitis.

Glass foreign body particles present a slightly different problem. If there is a large glass fragment present as a foreign body, it should be removed. If the glass contains sufficient lead, it may be possible to visualize the particle on roentgenograms. This will permit accurate localization and accurate surgical approach to the particle. If, however, the glass fragment is a small one and is located in a nonfunctional area of tissue, it should be allowed to remain undisturbed. Discretion is certainly the better part of valor in deciding whether or not to attempt to locate and remove tiny glass particles in the tissues, since their removal may present an impossible technical problem. Very often a secondary foreign body reaction with localization of a small foreign body abscess or pustule immediately beneath the skin will render delayed removal of a tiny glass splinter or fragment much simpler from the technical standpoint.

Location of the foreign body, whether glass or metal, in a particular site is an indication for immediate surgical action: (1) All foreign bodies which by their location may be presumed to have penetrated a body cavity or a viscus in their course through the tissues should have immediate surgical exploration of the tract created by the foreign body from its point of ingress to its point of egress or lodgment in the tissues. (2) Aspirated foreign bodies in the respiratory passages demand immediate removal. (3) Foreign bodies should be removed from the eye as soon as possible.

Certain other locations of foreign bodies, particularly metallic foreign bodies, are indications for surgical removal; but in such cases the procedure is not an emergency. Surgery should be performed as an elective procedure with an accurate plan. These foreign body locations are (1) over a bony prominence just beneath the skin; (2) over or adjacent to moving joints, as, for example, finger joints, olecranon surface of the elbow, the patellas, the toes, the mallecli of the ankle; (3) on weight-bearing surfaces, such as the plantar surface of the foot or the gluteal area if the foreign body is of sufficient size; (4) proximity to or impingement upon a major arterial trunk; (5) impingement upon a peripheral sensory nerve trunk; (6) tissues of the face. While foreign body in the face may not cause impairment of function, the patient's continuous awareness of its presence and his concern about the cosmetic effect will dictate removal if this can be accomplished with minimum scarring or with reduction of the cosmetic defect.

Foreign bodies in certain locations usually require no therapeutic action. (1) Those located in the extremities, except for those on weight-bearing surfaces, at moving joints or impinging upon major arterial or nerve trunks, need not be removed. (2) Ingested foreign bodies usually will pass through the intestinal tract and are recoverable from the patient's stool if careful observation is maintained. Removal by endoscopic manipulation or operative approach is indicated when roentgenograms show no progress of the foreign body along the intestinal tract or if signs of bowel or peritoneal irritation develop.

In general, then, organic foreign bodies require immediate removal, whereas nonorganic foreign bodies do not represent an emergency surgical problem and can usually be evaluated and dealt with on an elective basis with an accurately planned surgical approach.

Abstracts of Current Literature

Clinical Toxicology

A Study of the Action of Silica Particles on Macrophages in Vitro. B. Pernis, E. C. Vigliani, and L. Monaco. Med. lavoro 51:3 (Jan.) 1960.

This research represents a further attempt in clarifying the fibrogenic mechanism of silica. When macrophages in culture are challenged by quartz or tridymite particles, they eagerly ingest them and rapidly degenerate. Apparently, through their disintegration, fibrogenic factors are set free. The morphological alterations presented by the macrophages under the silica action are somewhat similar to those of cells treated in vitro with homologous antigen. This parallel is used by the authors to point out a possible complement activation by silica as the initiating factor for the cellular necrosis.

A group of experiments to discriminate the relative importance of simple chemicophysical or enzymatic processes as mediator of silica toxicity seems to favor the enzymatic hypothesis. Actually, several complement inhibitors like 48/80, glutathione (GSH), TAMe protect the macrophages against the silica particles.

Presented as an alternative to the involvement of the complement enzyme is the theory of a nonspecific esterase activated by silica particles in macrophages. This esterase, independent from the complement enzymatic system, once activated, may initiate the lysis of the macrophages, a process which appears to be critical for the liberation of fibrogenic factors. —M.C.B.

Chemical Cyanosis—Causes, Effects, and Prevention. J. M. Wetherhold, A. L. Linch, and R. C. Charsha.* Arch. Environ. Health 1:353 (Oct.) 1960. (*Medical Division, Industrial Hygiene Laboratory, Chambers Works, E. I. du Pont de Nemours and Co., Inc., Penns Grove, N. J.)

The cyanotic state may be produced by respiratory and circulatory abnormalities within the lung and by chemicals that displace oxygen or block the reaction between hemoglobin and oxygen. With respect to the latter, most of the aromatic amino and nitro compounds are probably not cyanosis producers; however, many of their oxidation or reduction derivatives are cyanogenic. The aniline derivatives produce cyanosis more rapidly than the nitro compounds. The chloroanilines are effective cyanosis-producing agents. By means of a micromethod (described) in which one drop of blood was used, it was shown that patients with 30% methemoglobin values resulting from exposure to toluidines and nitroanilines had no clinical signs of cyanosis. It was also shown that persons with heavy exposure to nitrobenzene had neither clinical evidence of cyanosis nor abnormal methemoglobin concentrations. Therefore, visible cyanosis signs may be absent despite the fact that sufficient hemoglobin alteration has occurred to produce signs of central nervous system anoxia. Dramatic recovery after injections of small quantities of methylene blue has been observed. High environmental temperatures, alcohol ingestion, and sulfides promote the development of cyanosis.

The acute and chronic phases of chemically induced cyanosis are discussed. Likewise, exposure control and preventive methods are reviewed. The latter consist of respiratory protection, rotation of the workers, limited exposures, and various types of body-protective clothing. The value of thorough washing in the event of skin contact is emphasized. —L.H.M.

Uber die Asbestose (Asbestosis). J. König.* Arch. f. Gewerbepath. u. Gewerbehyg. 18:159, 1960. (*Pathologisches Institut, Allgemeines Krankenhaus St. Georg, Hamburg, Germany.)

After a thorough literature review on the pathogenesis of asbestosis, the author presents 36 cases (13 male, 23 female) with an autopsy diagnosis of asbestosis collected over the past 20 years from general autopsy material. In only seven cases was asbestosis the main cause of death. In all others, asbestosis was recognized clinically rather late or found only incidently at autopsy. For all cases, occupational histories, clinical data, general pathology findings, and microscopic lung findings, are presented and discussed in detail. From the microscopic findings, the author drew conclusions about the pathogenesis of asbestosis, rejecting the theory of a diffuse attack on the lung parenchyma in favor of bronchiolar reactions with peribronchiolar fibrosis (bronchiolar phase) which finally lead to secondary rigid fixation of the parenchyma and diffuse fibrosis (parenchymal stage). The bronchiolar phase would account for the occurrence of marked functional impairment in cases with slight x-ray changes; however, the reverse situation remains still unexplained. Bronchitis obliterans and bronchiectasis were seen to be the cause for postinfectious irritation and functional impairment. These, in leading to considerable epithelial regeneration, are considered to provide eventually the basis for malignant degeneration. On account of their general distribution, such regenerative foci increase greatly the probability of the development of pulmonary cancer. This and not a primary cancerogenic effect of the asbestos could explain the frequency of lung cancer in asbestosis.

In 6 out of 13 males (46%) and 5 out of 23 females (27%), carcinoma of the lung or pleuroendothelioma was found. In contrast to this, the general autopsy material seen at the same hospital during the past 10 years showed pulmonary and plural malignancies only in 11.6% of the male and 2.1% of the female patients. In 4 of the 11 cases of carcinoma the neoplasms were

Abstracts

pleuroendotheliomas. Extrapulmonary carcinoma, especially of the stomach and peritoneum were also found at a rate much higher than that of the general autopsy material. This was true particularly for the peritoneal cancer, which was found in 3 cases of asbestosis (8.3%), compared with only 0.1% among the general autopsy material. Because of these latter figures and the fact that hematogenous generalization of asbestos bodies has been demonstrated, the author raises the question whether the peritoneal carcinoma in asbestosis should not be considered as a complication directly related to asbestosis. —O.P.P.

Industrial Hygiene Controls

Hygienic Guide Series: Acetonitrile, Diethylamine, Nitropropane, Diethylene Triamine, and Tetrachloroethylene. Hygienic Guides Committee of the AIHA, Chairman: D. W. Fassett.* Am. Indust. Hyg. A. J. 21:265 (June) 1960. (*Laboratory of Industrial Medicine, Eastman Kodak Co., Rochester, N. Y.)

Acetonitrile (methyl cyanide, ethanenitrile) is given a suggested MAC of 40 ppm, which is at or near the olfactory threshold. Even though the short exposure tolerance is considerably above the recommended MAC, there have been cases of human intoxication from exposures to unknown but high concentrations inside tanks.

Diethylamine is commonly used in the manufacture of accelerators, insecticides, emulsifiers, and pharmaceuticals and is readily recognized by its ammoniacal odor, which is irritating to the mucous membranes. The suggested MAC of 25 ppm is one which should not be too difficult to obtain and probably would not be casually exceeded.

Nitropropane has a recommended MAC of 50 ppm. This is based on observations with 2-nitropropane, and it seems reasonable to extend the same limit to 1-nitropropane, since they are similar in toxicological and physical properties. Both the liquid and vapor can produce cyanosis, and the vapor also produces respiratory tract irritation. Since the odor is not detectable at the allowable concentrations, it has poor warning properties; hence, reliance must be placed on air analyses. This chemical has been used as a solvent for special lacquers and dopes.

Diethylene triamine is a highly sensitizing chemical for which no recommended atmospheric concentration is suggested. Both acute and chronic health hazards are severe. High concentrations produce skin and eye damage. Pulmonary and cutaneous sensitization can result from prolonged exposure to lower concentrations. Crosslinking of proteins with bifunctional amino groups probably is the basis of the sensitization reaction.

Tetrachloroethylene, frequently referred to as perchlorethylene, has been given an MAC of 200 ppm. It is suggested that this may be too high for a prolonged exposure, although 200 ppm is not an acutely toxic level. This nonflammable solvent has wide use as a cleaning agent. —E.C.R.

The Hazards to Health in the Hydrogenation of Coal: III. The Industrial Hygiene Studies. N. H. Ketcham* and R. W. Norton. Arch. Environ. Health 1:194 (Sept.) 1960. (*Union Carbide Chemicals Co., Charleston, W. Va.)

To evaluate personnel contact with potential skin carcinogens, various industrial hygiene studies of the industry were undertaken. Weil, in a previous publication, indicated the likelihood of the development of skin cancers from products of large-scale hydrogenation of soft coal. Through the release of dusts, vapors, fumes, and mists in the industrial operation, it would appear that these physical states may contain carcinogenic oil fractions.

To test this hypothesis, it became necessary to determine where such materials escaped and also to measure the concentration accurately. Once this was known, essential engineering and sanitation controls could be instituted.

The proposed atmospheric studies took into consideration the fact that some 200 individual chemicals could be identified during the process of coal hydrogenation. Therefore, total air analysis was found to be unreasonable, and an attempt was made to find a "tracer" which would likely be present in all of the fractions. The "tracer" selected was 3,4-benzpyrene. It met the proposed criteria of the study group in that it was a carcinogen and it could be quantitated.

Since 3,4-benzpyrene was particulate in form, atmospheric collection was by filter-paper equipment. Analysis was done by two methods each "giving results in the correct order of magnitude." Samples were collected within the plant as well as in residential areas. Reported values ranged from 0.0 to 1,870 μg of "tracer" per 100 cu m of air. Present knowledge did not permit correlation of these values to the degree of health hazard. Such studies, however, did pinpoint potential areas needing further controls.

In addition to air sampling, either by mechanical air samples or by collecting "fallout," the skin of plant employees was examined under 2,537 A ultraviolet light. Through this technique, the degree of skin contamination could be readily detected. By these studies, certain major problem areas were defined. These included treatment of hot residue, steam blowdown of hot oil fractions, and discharge steam from ejection jet. Minor areas included the laboratory, cleaning of hand tools, worn packings on piston rods of large paste pumps as well as vent lines and stacks. Complete engineering controls were not accomplished owing to curtailment of large-scale operation of the plant before study was done.

To reduce skin contact, a personal protective-clothing program was instituted. Shower and locker room facilities were redesigned, and ultraviolet light inspection of the skin after bathing was instituted. The use of protective clothing and

the encouragement of personal hygiene were the first line of defense. —L.W.S.

The Health of Workers in a Plant Making Highly Dispersed Silica. H. Volk.* Arch. Environ. Health 1:125 (Aug.) 1960. (*State Board of Health, Saakegin/Rhein, Germany.)

Since 1944, a plant in Germany has been producing an amorphous "highly dispersed chemically pure silica under the trade name of Aerosil."

The product is made up of spherical particles measuring 5-40 μ containing 99.8% SiO_2. Chemical analysis shows that traces of aluminum, iron, and titanium are present. The material is obtained by hydrolytic decomposition of silicon tetrachloride in an oxyhydrogen flame.

It was anticipated that pulmonary changes may occur on prolonged exposure to this dust. From 1944 to 1958, chest x-rays were taken every six months and since 1958 every year. Highest dust concentrations were in the furnace room as the bags were filled and loaded. During the filling process, dust concentrations varied from 15 to 100 mg per cubic meter, while during the bagging procedure dust concentrations were between 2-6 mg per cubic meter. The author estimates that daily dust intake for the working day was 120 mg and that 25 gm was inhaled during the year. Dust respirators were available.

The dust concentrations and x-ray findings were studied for the period 1947-1959. During this time interval, the author did not find a single case in which any change was noted in respiratory organs which could possibly have been caused by contact with the product. —L.W.S.

Medical Care Administration

Hospitals and Doctors Can Be Happy Though Married. J. M. Danielson* and D. N. Danforth. Mod. Hosp. 95:98 (Aug.) 1960. (*Evanston Hospital Association, Evanston, Ill.)

Although medical care is better than ever, the free-enterprise system under which it has grown suffers increasing jeopardy from bureaucratic control. Public criticism, though powered by rising costs of hospitalization, is mainly directed at the medical profession because the public implicitly accepts the marriage of doctors and hospitals. In spite of the growing threat to voluntary insurance, physicians and hospitals continue jealously to guard their independence.

It is necessary that hospital administrators and physicians critically reappraise their mutual faults and failures. The hospital must recognize the physician as its greatest public relations asset and must improve communication with him. Physicians must be more intimately apprised of the details of hospital management. Physicians should regard hospitals not as a threat to their private practice but as their greatest ally. They should assume a greater share of responsibility for the whole hospital's problems.

The public will not grant a divorce in this marriage. Every effort must be made to evolve the essential teamwork that created the great hospitals of the past. The Mayo Clinic and The Johns Hopkins Hospital succeeded by reason of close and mutual understanding between the physicians and the management of the great institutions. This must be done at the local level of every community hospital if the voluntary way is to be preserved. —J.D.W.

Medical Coordination in Pennsylvania. H. Robertson.* Virginia M. Month. 87:583 (Oct.) 1960. (*Philadelphia, Pa.)

The Pennsylvania Medical Society at its annual meeting in 1959 announced a plan to deal with the increasing costs of modern medical care. It was stated that success would depend upon the cooperation of organized medicine with third parties wherein all interested partners concede certain privileges for the good of all.

This event was made remarkable by its implementation initially by the Blue Cross Plan of Philadelphia and the Philadelphia County Medical Society. Credit must be given to the Commonwealth Insurance Commissioner, who handed down his adjudication to the effect that the hearings established beyond any doubt that unnecessary utilization of hospital service can be substantially reduced.

Thus, the Physician's Review Board was born to work as an independent body with Blue Cross. The deliberations of this entirely professional organization of 36 senior physicians is assisted by the staff of Blue Cross. The judgments are conveyed appropriately to the paying agency and to the managing physicians.

Blue Cross has long paid bills which, it was frankly felt, were not in accordance with subscriber contracts. Efforts to use professional auditors or medical referees have failed to be acceptable or effective. Grievance committees and similar mechanics of the medical society have also failed to produce an adequate solution. The new plan has succeeded.

The Board is convinced that traditional free and easy habits waste a great deal of Blue Cross reserves. Physicians can change these habits when they become convinced that government will make the change for them unless they use their own initiative. —J.D.W.

Steelworkers May Go It Alone for Health Care. Feature Report. Mod. Hosp. 95:65 (Oct.) 1960.

The United Steelworkes of America may choose to test other approaches toward providing 1,200,000 steelworkers and their families with medical care if benefits under existing plans cannot be made more satisfactory.

Four major problems were pointed up in a report of the Union's Insurance, Pension, and Unemployment Benefits Department presented at the

Abstracts

1960 annual convention in Atlantic City. The points cited were (1) inability of the steelworkers to get fee schedules accepted as full payment, (2) rising costs of insurance, (3) evidence that prepayment plans with group-practice clinics may offer greater benefits at less cost, and (4) failure of existing programs to guarantee the quality of medical care.

Since development of a new program would be complex, a series of small pilot projects might be undertaken in selected areas. The difficulties of obtaining capital funds for construction of needed facilities may be solved by help from various sources, including loans from union pension reserve funds, loans from steel companies, government grants, and philanthropy. —J.D.W.

Third Party Medicine—A Modern Gordian Knot. D. D. Harkins. Kentucky Law J. 48:141 (Fall) 1959.

One of the most pressing problems of organized medicine has been the specter of the "third party." This often interjects laymen between the physician and the patient to pay bills but also to exert some control over the type of care rendered. While the profession has made great progress in the science of medicine, proportionately little time and progress has been made toward helping the patient meet the cost of medical care. Into this void have stepped laymen in the form of insurance, trusts, cooperatives, and labor organizations.

It is the scope of this paper to examine the idea of "third party medicine" and to review the counterattack by organized medicine, particularly in the light of Kentucky statutes and decisions. It is observed that the interjection of a third party into the patient-physician relationship, while making changes, is not necessarily bad. What the courts, statutes, and, therefore, organized medicine must require of any plan is that there be no interference by laymen in the diagnosis and treatment of the patient. —J.D.W.

Dermatology

The Sunlight Factor in Aging and Skin Cancer. J. B. Howell.* Arch. Dermat. 82:865 (Dec.) 1960. (*Medical Arts Building, Dallas 1, Texas.)

Ultraviolet radiation of 3,200 Ångstrom units and shorter in sunlight is believed to be the cause of skin cancer and aging of the skin in man. This is based on experimental production of malignant tumors in rats and mice by these wavelengths, as well as on four clinical observations: (1) predilectional localization of skin cancer to exposed sites; (2) greatest incidence in geographical areas that receive the greatest insolation; (3) greatest incidence among outdoor and rural workers; and (4) higher frequency in light-skinned than in dark-skinned persons.

The primary site of action of the ultraviolet radiation may be the subpapillary vascular plexuses of the dermis, which, after injury, disturbs the nutrition of the overlying epidermis and causes aging of the skin, keratoses, and eventually squamous and basal-cell epitheliomas in susceptible persons. Light-skinned persons who tan poorly should avoid the sun or take protective measures. —M.M.K.

A "Triple-Test Plan" for the Serologic Diagnosis of Syphilis—a Modern-Day Approach. C. M. Carpenter,* J. N. Miller, and R. A. Boak. New England J. Med. 263:1016 (Nov. 17) 1960. (*University of California at Los Angeles School of Medicine.)

A practical triple-test plan is suggested for the serologic diagnosis of syphilis. A Venereal Disease Research Laboratories slide-flocculation test is carried out on all sera as a screening precedure. Reactive or weakly reactive sera are then subjected to the Reiter-protein complement-fixation test, which, when positive, confirms present or past syphilis. If the Reiter-protein complement-fixation test is nonreactive, then the Treponema pallidum immobilization test may be used to rule out biologic false positives. —M.M.K.

The Hazards to Health in the Hydrogenation of Coal: IV. The Control Program and the Clinical Effects. R. J. Sexton.* Arch. Environ. Health 1:208 (Sept.) 1960. (*P.O. Box 2831, Charleston 30, W. Va.)

In the hydrogenation of coal to produce pitch, coal tar, and high-boiling polycyclic aromatic chemicals, one or more carcinogens are formed, capable of causing skin cancer in laboratory animals. Heavy exposures to these materials are capable in less than a 10-year period of producing precancerous lesions and malignant neoplasms in man. Of 359 men employed in a coal hydrogenation plant over a nine-year period, 10 developed squamous and basal-cell epitheliomas, an incidence 16-37 times greater than expected. The shortest exposure prior to development of cancer was nine months. —M.M.K.

Hazards in the Use of Isopolyesters As Maintenance Coatings. R. W. Stephenson* and L. B. Fosdick. Am. Indust. Hyg. J. 21:522 (Dec.) 1960. (*Oronite Chemical Co., San Francisco, Calif.)

In the mixing and application of styrene-modified polyester resins, there are toxicity hazards as well as fire hazards. The chief toxicity hazard is acute styrene poisoning, manifested by eye and nose irritation, nausea, vomiting, anorexia, and general weakness. Contact dermatitis may be caused by the following materials: styrene, which is used to modify and dilute the resin; acetone, which may be used to clean the contaminated skin; organic peroxide catalysts, such as methylethylketone peroxide and benzoyl peroxide; and cobalt naphthenate, an accelerator. Contact with dimethylaniline, another accelerator, should be avoided because it is a central nervous system depressant and is readily absorbed through the skin. Industrial hygiene control measures include ven-

tilation or respirators, safety goggles, neoprene or polyethylene gloves and aprons, barrier creams, and good housekeeping.

The organic peroxides are strong oxidizing agents and should be used and stored with care. Cobalt naphthenate and dimethylaniline decompose rapidly and may ignite in the presence of an organic peroxide, unless they are first mixed with the polyester resin. Styrene vapor is flammable in certain concentrations. —M.M.K.

Patch Test Study to Determine Cutaneous Reaction to New Compounds. J. V. Klauder.* Arch. Environ. Health 1:407 (Nov.) 1960. (*Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pa.)

The primary irritancy and allergenicity of new products can be predicted by several procedures: the prophetic patch test of Schwartz and Peck, the repeated insult method of Draize and Shelanski, the patch test combined with usage test, and the open test with repeated applications. The number of subjects varies with the test, from 50 to 200.

In addition to primary irritation and allergic hypersensitivity, another reaction, the fatigue reaction, or exhaustion phenomenon, may be observed in patch test studies. The fatigue reaction is an accumulative irritant action which occurs only after repeated exposure. Considerable care is required to differentiate the fatigue reaction from allergy. —M.M.K.

Experimental Toxicology

Chronic Ingestion by Dogs of Methyl-Bromide Fumigated Food. I. Rosenblum,* A. A. Stein, and G. Eisinger. Arch. Environ. Health 1:316 (Oct.) 1960. (*Albany Medical College, Albany, N.Y.)

Twenty-two beagle dogs of both sexes were divided into groups and given approximately 150, 75, or 35 mg/kg/day of methyl bromide in food fumigated with methyl bromide or 100 mg/kg/day of bromide as sodium bromide. After one year, no, or only minimal, evidence of bromide intoxication was noted with the exception of the group receiving the highest dose of bromide in the fumigated food. In only one of the three dogs that died could the cause of death be related to bromide ingestion, and even this relationship was not clear. The studies suggest that fumigated food containing as much as 75-100 ppm of bromide could be ingested by man without hazard. This incorporates at least a 100-fold safety factor over the dose found safe in animals. —R.E.E.

Eye Irritants Formed During Photo-Oxidation of Hydrocarbons in the Presence of Oxides of Nitrogen. E. A. Schuck* and N. A. Renzetti. J. Air Pollution Control A. 10:389 (Oct.) 1960. (*Stanford Research Institute, South Pasadena, Calif.)

After ultraviolet irradiation of individual hydrocarbons in the presence of nitrogen dioxide, two reaction products—formaldehyde and acrolein—were found to be eye irritants and to account for the majority of the observed eye irritation found in the photo-oxidized systems studied. Epoxides, most aldehydes, ketones, nitrites, ketene, ozone, alkyl nitrates, and acyl nitrates were not eye irritants at the concentrations present. Terminal olefins, in general, led to the greatest amount of irritation. Internal olefins were of less importance in the formation of eye irritants, in spite of their rapid rate of reaction. Saturates did not contribute to eye irritation because of their slow rates of reaction. —R.E.E.

An Abnormal Serum Protein in Experimental Poisoning By Cardmium and Other Metals. D. J. Lawford.* Nature, London 187:946 (Sept. 10) 1960. (*Medical Research Council, London Hospital, England.)

A low molecular weight protein is found in the urine of men exposed for many years to cadmium fumes. An abnormal serum protein has now been isolated from the albino rat after the intra peritoneal subcutaneous injection of 1 mg/kg of cadmium and various other metals, some toxic and some present in trace amounts in the body. The response of animals to the metals after 24 hours with respect to protein production is in the following order: mercury > beryllium, cadmium, copper > manganese > chromium, nickel. Cobalt, lead, and iron did not induce the formation of this protein. The observation that mercury and cadmium salts induce the protein production in the serum of rats and can also give rise to proteinuria in man may help to clarify the mechanism of metal poisoning and proteinuria. —R.E.E.

The Metabolism of Mercury in the Rat Studied by Isotope Techniques. A. Rothstein* and A. D. Hayes. J. Pharmacol. & Exper. Therap. 130:166 (Oct.) 1960. (*University of Rochester School of Medicine & Dentistry, New York.)

The metabolism of Hg was studied in rats after i.v. and i.m. injections of mercuric nitrate (Hg^{203}) in saline. The liver acts as a reservoir for Hg for the first few days after i.v. injection but is rapidly cleared by fecal excretion, and the kidney then becomes the major site of deposition. After about two weeks, 85% to 90% of the total body burden is found in the kidney, and about 66% of the Hg is subsequently excreted via the urine. In the animals injected intramuscularly, the site of injection acts as a reservoir, and liver levels are low. Clearance from this site takes about two weeks after which most of the Hg is localized in the kidney. Whole body counts indicate three clearance phases: a rapid phase involving 35% of the dose and lasting a few days; a slower phase involving 50% of the dose with a half-time of 30 days; another slow phase of 15% of the dose with a 100-day half-time. The slow phases represent mainly clearance from the kidney, and all were independent of ad-

ministration route. With different dose levels (5 to 50μg/rat) clearances were about the same percentagewise. The low levels of Hg in the brain fail to explain the effects of the metal on the CNS, as observed in chronic Hg poisoning.
—R.E.E.

Effects of Adenine on Blood Disease Due to Benzene Poisoning. W. Paolino* and E. Vercellino. Panminerva Med. 2:5 (Jan.) 1960; Occ. Hyg. Abstr. 35:647 (July) 1960.

Studies in rabbits suggest that large doses of adenine may have a protective effect in the leucopenia of chronic benzene poisoning, but additional studies are needed to confirm this.—R.E.E.

Role of Polyoxyethylene Sorbitan Monostearate in Skin Carcinogenesis in Mice. G. Della Porta.* P. Shubik, K. Dammert, and B. Terracini. J. Nat. Cancer Inst. 25:607 (Sept.) 1960. (*Chicago Medical School, Chicago, Ill.)

A detailed record of tumors induced in mouse skin by repeated applications of 'Tween 60 (polyoxyethylene sorbitan monostearate) with and without a prior single application of a carcinogenic hydrocarbon is reported. Most tumors induced subsequently regressed. Only about 3% progressed to carcinomas. 'Tween 60, at a dose of 60 mg administered twice weekly or daily, was effective as a promoting agent. When given alone at the same dosage, there was an appreciable number of tumors, with a far longer latent period. There was a marked dosage response with an apparent threshold. The effects of dosage, different initiating agents, interval between initiation and the 'Tween applications and the individual caging of animals are described. The nature of the activity of 'Tween 60 is compared with that of croton oil. It seems to have a promoting activity comparable to that of croton oil. Since the quantity of 'Tween 60 needed to induce activity is so large, this may be a gross physical phenomenon quite different from the action of other chemicals in skin carcinogenesis, analogous perhaps to the induction of sarcomas by implantation of plastics.
—R.E.E.

The Physiological Response of Animals to β-Nitronaphthalene. J. F. Treon* and F. P. Cleveland. Arch. Environ. Health 1:324 (Oct.) 1960. (*Atlas Powder Co., Wilmington, Del.)

The oral LD_{50} of β-nitronaphthalene for rabbits and rats is 2.65 and 4.4 gm/kg, respectively. Degenerative and necrotic lesions were induced in the liver, kidneys, and brain. Methemoglobin formation, large numbers of Heinz bodies, and an increase in peripheral blood clotting time were induced in the rabbits. Multiple oral doses of approximately one-tenth the LD_{50} induced fatalities in rabbits but not in rats. Similar but less severe changes than seen in the single-dose studies were induced. Clotting time was not altered in the multiple-dose studies. Some percutaneous absorption was apparent when the skin was abraded and the compound applied as a peanut oil paste. Absorption from the respiratory tract was essentially nil in cats, guinea pigs, rats, and mice exposed for seven hours on each of 50 days to air containing 1.91 μg/liter of β-nitronaphthalene. In the oral studies, conjugation products with sulfuric and glucuronic acid were found in the urine of rabbits.
—R.E.E.

Surgery

Treatment of Acute Thermal Burns of the Face. J. L. Bell,* AM. J. Surg. 98:923, 1960. (*Chicago, Ill.)

The author points out that the face is commonly subjected to thermal injuries because of its exposed, unprotected location and that the depth of burning is dependent upon the intensity, duration, and location of the heat. He also stresses the fact that many thermal injuries involve the entire thickness of the skin and that in some instances deeper structures are damaged. Considerable emphasis is placed on the early care of a local burn wound so as to avoid infection and achieve early healing. If these early aims are not accomplished, the problems of reconstruction are compounded.

Rightfully, emphasis is placed upon the early evaluation of the burned patient's respiratory function. In extensive burns about the head and neck, marked edema can occur within hours after injury. Labored respiration, coughing, hoarseness, cyanosis, and air hunger should offer sufficient warning of impaired respiratory exchange for the responsible surgeon to consider early tracheotomy. It is suggested that prophylactic tracheotomy be carried out in all patients with whole-thickness burns about the face and neck even though they fail to show initial evidence of tracheobronchial irritation.

The author stresses the generally held conception that burn shock occurs if more than 15% of the body surface is involved in the thermal assault. He goes on to say that this phenomenon should be anticipated in patients with head and neck burns involving less than 10% of the body surface. He also points out that disorientation, which is a common manifestation of shock, is frequently misinterpreted as pain. The importance of maintaining proper fluid and electrolyte balance by close surveillance of the hourly urine output is stressed.

The author advocates the use of early cleansing with soap or a mild detergent and sterile water in the initial care of the burned surface. Emphasis is placed on the importance of the strictest aseptic precautions in this early stage of treatment. The removal of loose tags of tissue and debris is accomplished with the utmost care. Because it is difficult to apply a satisfactory dressing in facial burns, the author favors the exposure method of treatment. The local applications of ointments or medications should be avoided if the exposure

method is used. The author emphasizes that if infection, maceration, and mechanical irritation are avoided superficial second-degree burns heal without scarring in two weeks.

It is pointed out that because of the great vascularity of the face eschars start to soften and separate at the edges between 7 and 10 days after the burn has been incurred. At this point, the eschar no longer serves as a protective barrier against bacterial invasion. The application of sterile moist dressings can hasten the separation of the nonviable tissue from the underlying vascular surface. It is further emphasized that formal surgical excision of facial eschars is neither necessary or advisable because of two factors: (1) The natural separation of the whole-thickness slough is rapid. (2) Such a procedure may result in needless sacrifice of underlying subcutaneous or deeper tissue. It is suggested, however, that scissors can be used frequently to divide tough avascular strands between the necrotic skin and the deeper tissue. The removal of this necrotic tissue will convert a dirty wound into a surgically clean wound within 5-10 days.

According to the author, most patients having full-thickness burns are ready for skin grafting within three weeks after the thermal injury. Whereas only split-thickness skin grafts can be used to cover granulating wounds, full-thickness grafts are used for reconstructive procedures when the burns are well healed. Early closure of the original injury enhances the ultimate restoration of function and appearance of the burned part.

The importance of adequate nutrition in the management of burns is stressed by the author. He believes that after the period of burn shock the severly burned patient should be placed on a high-protein, high-calorie diet. Supplementary feeding of high-protein formula may be introduced via a nasogastric tube if the patient is unable to take the required amounts orally. Needed emphasis is placed on the fact that plasma and other forms of intravenous proteins are of no value in helping to correct protein deficiency.

Prophylaxis against tetanus and the use of systemic and local antibiotics is discussed. —J.T.A.

Noise and Hearing

Relative Hearing Levels and Types of Hearing Loss Among Four Selected Groups of Air Force Personnel. L. L. Kopra,* D. T. Pedrini and R. W. Fullington. SAM Report 59-51, School of Aviation Medicine, U.S. Air Force, April, 1959. (*University of Texas, Austin, Texas.)

One hundred twenty-five male Air Force personnel ranging in age from 18 to 44 years were given pure-tone air and bone audiometric tests. One group consisted of 25 non-noise-exposed men. The other three groups consisted of noise-exposed persons classified according to Air Force Regulation 160-3: 25 Class A—no hearing loss greater than 15 db in either ear from 500 to 6000 cps; 50 Class B—more than 15 db hearing loss in either ear but not averaging more than 15 db for 500, 1000, and 2000 cps; and Class C—average loss in either ear of more than 15 db for the three speech frequencies.

Results indicated that there were no significant differences between right and left ears of subjects within groups. The Class A thresholds were within a few decibels of the American Standard reference normal. The Class B group deviated from the Class A group only at 3000, 4000, and 6000 cps. Except for the Class B group at 4000 and 6000 cps, the Class C group was significantly different from the other groups at all test frequencies. Thirteen percent of the Class B and C groups had either conductive or mixed-type hearing loss, while the remaining 87% had perceptive-type losses. Thirty-five of the 75 persons in Class B and Class C groups expressed a preference for an ear, and of these 25 persons 25 chose the better ear correctly. —R.G.H.

Factors Influencing the Evaluation of Ear Protective Devices. R. G. Hansen* and D. T. Blackstock. WADC Technical Report 57-772. Wright Air Development Center, May 1958. (*School of Aviation Medicine, U.S. Air Force, Brooks Air Force Base, Texas.)

The purpose of this study was to determine the number of subjects and the number of repeat measurements necessary to obtain a reliable value for the average attenuation on an earplug under specific controlled conditions. Attenuation values for the V-51R earplug were obtained at nine frequences for 20 subjects on each of five separate occasions. The method established by the American Standards Association for determining "real-ear" attenuation of ear protectors was employed, and this research was a trial study of the method. Results indicate that satisfactory data could be obtained with three repeat measurements on 10 subjects. Approximately the same results would be obtained with 6 subjects making five repeat measurements or one measurement on 15 subjects. —R.G.H.

The Mechanism of Bone Conduction. G. W. Allen* and C. Fernandez. Ann. Otol. Rhin. & Laryng. 69:5 (March) 1960. (*303 E. Chicago Ave., Chicago, Ill.)

Bone conduction, that is, stimulation of the inner ear by means of a vibrating transducer applied to the head, has been ascribed to two separate though complementary processes that may be called compressional and inertial. In compressional bone conduction the sound energy simply travels through the bone and produces alternate compression and rarefaction of the otic capsule; the extent of the movement of the basilar membrane resulting from this energy will depend on factors such as the relative stiffness of oval

and round windows and the effective impedance of the middle ear. The fundamental concept in inertial bone conduction is that, because of the inertia of the ossicles, there results a relative movement of the ossicles with respect to the otic capsule when the transducer shakes the head; hence the actual stimulation of the basilar membrane can then be explained in the same way as in ordinary air conduction. In a series of experiments involving changes in position of the transducer, loading ear drums with skin grafts, and plugging the external meatus, these authors obtain results that support their thesis that "while inertial forms of bone conduction do exist, the only important mode of simulation is compressional." All the important clinical and experimental phenomena of bone conduction are said to be consistent with this thesis. —W.D.W.

Annoyance Threshold Judgments of Bands of Noise. W. Spieth.* J. Acoust. Soc. America. 28:872 (Sept.) 1956. (*Operational Applications Laboratory, Air Force Cambridge Research Center, Bolling Air Force Base, Washington 25, D.C.)

Annoyance threshold judgments to bands of noise were obtained by exposing a person to noise for three minutes and asking him to adjust the intensity to the level which, if any louder, would annoy him if it were present most of the time where he was working.

In one experiment, 21 persons made annoyance judgments about 13 bands of noise which covered the frequency range of 50 to 13000 cps and subsequently made sets of equal loudness matches. No differences were found between the annoyance threshold curves and the equal loudness curves. In another experiment, each of 162 persons made one annoyance judgment. By transferring the annoyance thresholds into equivalent loudness terms, the resultant annoyance threshold curve varied reliably with frequency only in that the threshold of the highest band was reliably lower than those on the lower frequency bands. Office workers who had previously worked in noisy situations as well as those working in noisy situations at the experiment gave thresholds about 15 db higher than did people who had only worked in office-type situations. Within the group who had worked only in quiet situations, those who tried to imagine themselves in an actual working situation gave thresholds that averaged 15 db higher than the thresholds of those who did not. —R.G.H.

Experiments on Vigilance: Performance on a Simple Vigilance Task in Noise and in Quiet. H. J. Jerison* and R. A. Wallis. WADC Technical Report 57-318, Wright Air Development Center, June, 1957. (*Aero Medical Laboratory, Wright-Patterson Air Force Base, Ohio.)

Twenty male undergraduate students worked on a simple vigilance task without interruption for one and three-fourths hours in quiet (79 db). The subjects were required to press a switch when they saw the hand on a clock take a double jump, i.e., a 20-degree step instead of the regular 10-degree jump. The performance function was a typical one found in such tasks. Performance dropped off rapidly after an initial high level. There was no differentiation between performance in noise and in quiet. This result is explained on the basis of the absence of the need for flexibility of attention for performance on such a simple "vigilance" task. —R.G.H.

Radiation

Plutonium Accumulation from Long-Term Occupational Exposure. H. Foreman,* W. Moss, and W. Langham. Health Physics 2:326 (May) 1960. (*Los Alamos Scietific Laboratory, University of California, Los Alamos, N. Mex.)

Tissue analysis on a patient who had been chronically exposed by inhalation to low-level plutonium aerosols provides data on the actual and relative concentrations of plutonium in various body tissues and allows a comparison of predicted and actual body burdens. Somewhat surprisingly, half of the plutonium was found to be in the liver. The skeleton contained about 36%. The highest concentration by far was in the pulmonary lymph nodes, with liver, lungs, and bone next in order. The unpredicted distribution probably resulted from the insolubility of the material and the circumstances of intake.

Existing excretion equations, which are applicable to somewhat different types of exposure, predicted body burdens from 0.019 to 0.034 μc. Actual body burden based on analysis of tissue aliquots was 0.018 μc. The choice of a critical organ for plutonium under these conditions of exposure is in doubt. —T.S.E.

Some Experiences with Irradiation Injury. J. W. Ferrebee* and E. D. Thomas. Radiology 75:1 (July) 1960. (*Mary Imogene Bassett Hospital, Cooperstown, N. Y.)

Several cases of intentional whole-body high-level radiation injury followed by bone marrow grafting in humans and dogs are presented. Doses range from 150 to 1,500 r. The humans presented had leukemia. One child survived an acute exposure of 1,000 r followed by infusions of fetal hematopoietic cells and adult bone marrow cells despite the fact that apparently neither of these grafts took. It seems that such doses are not necessarily uniformly lethal. A little girl with leukemia recovered from a whole-body dose of 900 r followed by an infusion of bone marrow cells from her identical twin. A male dog survived an acute radiation dose of 1,800 r followed by an infusion of a female's marrow cells. He is still alive and well with blood from a female. A group of nine dogs survived doses of 1,000 to 1,500 r well following marrow transfusions of autologous marrow, some of which had been

stored at minus 80° C in glycerol. One problem which has occurred with this treatment of radiation injury has been the failure of lymph node function. Intercurrent infection may produce a fatal outcome before lymph node function can recover. —T.S.E.

Strontium-90 in Man IV: The Strontium-90 Concentration in Human Bone Increased in 1958 and 1959, Will Probably Reach a Maximum in 1960. J. L. Kulp,* A. R. Schulert, and E. J. Hodges. Science 132:448 (Aug. 19) 1960. (*Geochemistry Laboratory, Lamont Geological Observatory, Columbia University, Palisades, N.Y.)

The cessation of nuclear testing in 1958 has been made it possible more accurately to determine some of the mechanisms of the fallout of strontium-90 and its uptake in man. This study began in 1953. Since that time, 9,000 samples of human bone of all ages and many parts of the world have been obtained. Since strontium-90 has been a part of the diet for only a relatively few years compared to the turnover time of bone mineral in humans, the concentrations of this isotope are much lower in adults than in children. Observed bone concentrations agree remarkably well with predicted values based on discrimination factors, the weight of calcium added to the skeleton at each age, and the average amount of strontium-90 in the diet. On the basis of a metabolic model developed from data in this study and referenced articles, projections of the strontium-90 concentration in bone are made for the 1-year-old, the 15-year-old, and the 26-year-old for the case of no further atmospheric testing. —T.S.E.

Radiation Environment in Space: Satellites and Space Probes Are Revealing the Kinds and Amounts of Radiation Men Will Encounter in Space. H. E. Newell* and J. E. Naugle. Science 132:1465 (Nov. 18) 1960. (*National Aeronautics and Space Administration, Washington, D.C.)

Before 1958, ionizing radiation was not considered to be a serious hazard in space travel. In that year, however, Dr. James A. Van Allen announced the discover of two belts of charged particles that are trapped by the earth's magnetic field and that constitute hazardous radiation regions. Presumably, any planet with the magnetic field would have similar belts. The inner belt consists mainly of high-energy protons. The significant radiation in the outer belt is electrons from 20 Kev to 100 Kev in energy. The hazard from these electrons is the soft x-rays that they produce.

The space traveler, then, faces several ionizing radiation hazards. Cosmic radiation in space amounts to 5 to 12 r per year. The inner Van Allen belt radiation intensity is about 24 r per hour. The outer Van Allen belt radiation intensity is about 200 r per hour. Solar flares of protons have produced radiation intensities up to 30,000 r per hour.

Project Mercury contemplates an orbit below the inner belt and therefore presents no problem with respect to ionizing radiation hazards. With present technology, it would seem that sufficient shielding could not be carried aloft to permit an orbit in either the inner or outer radiation belts. Beyond the outer radiation belt, radiation intensities are the 5 to 12 r per year from cosmic sources plus the probability of a solar flare of protons. The latter must be handled by a combination of appropriate shielding and solar flare prediction techniques.

NOTE: Readers should be careful about an occasional misleading or erroneous reference to radiation exposure standards in this article. —T.S.E.

Internal Medicine

Evaluation of the Heaf Tuberculin Test. A. B. Robins* and J. N. Daly. New England J. Med. 262:1008 (May 19) 1960. (*New York University College of Medicine, New York.)

The Heaf test is a multiple-puncture tuberculin test with few drawbacks. The risk of serum hepatitis is considered minimal. In fact, no cases thus far have been reported after more than 100,000 tests have been done in New York City and many more elsewhere. The Heaf test is more acceptable than the Mantoux to those giving as well as to those receiving the test. Less personnel and less equipment are required; the test can be done quickly, and there is more flexibility in scheduling. It is relatively free of local or systemic effects. The ease of interpretation has led to self-reading, and this appears promising.

The technique for testing is as follows: The skin of the forearm is cleansed with acetone. A drop of special PPD tuberculin with a concentration of 2 mg per milliliter is applied to the skin by a syringe with a 25-gauge needle attached. The apparatus is sterilized by covering the end-plate with alcohol and flaming it. The end-plate is then applied to the drop on the skin and the needles released. It is allowed to dry, and no dressing is needed. The test is read in 72 hours but may be left for a longer interval. Four grades of positive reaction are distinguished ranging from four or more papules to an induration of more than 10 mm in diameter. More than 100 tests can be given in one hour.

The initial cost of the apparatus is high, but it has a long life. Needles need not be replaced or sharpened until after 2,500 or more tests have been given. The PPD solution is inexpensive and will not deteriorate for one year.

For industry, since time lost from production must be kept at a minimum, the greatest drawback is the necessity for repeated visits for testing, interpretation, and x-rays when necessary.—S.H.S.

Bedside Diagnosis of Carotid Artery Occlusive Disease. S. N. Groch,* L. J. Hurwitz, I. S. Wright, and F. McDowell. New England J. Med. 262:705

Abstracts

(April 7) 1960. (*Cornell University Medical College, New York.)

The correct diagnosis of this condition can be established in 80% of the cases by bedside means, and cerebral angiography is not essential in the majority of cases.

The essential diagnostic features are a history of (1) an ipsilateral visual disturbance with contralateral sensory or motor deficit (occurred in 18%), and (2) somnolence (occurred in 15%). Given a patient with the above symptoms, one should search for telltale physical signs.

Horner's signal—It is an important one, may not be obvious, and is transient. It is better demonstrated in a dark room after instillation of 1% cocaine in both eyes.

Bruits—A contralateral intracranial bruit is most helpful in establishing the diagnosis.

Carotid Artery Palpation—This is unreliable if the carotid vessels in the neck are palpated, but palpation of the internal carotid in the pharynx is of great value. The pharyngeal pulse was found to be absent in 10 of 24 patients.

Retinal Artery Pressures—Ophthalmodynamometry is a relatively simple and extremely valuable diagnostic tool. Reduced pressure in the retinal artery on the involved side was found in 77% of cases.

The authors conclude that the bedside diagnosis of occlusive disease of the carotid artery can be established, and the most reliable measures are ophthalmodynamometry, and, after that, palpation of the internal carotid artery in the posterior pharynx. —S.H.S.

Totally Asymptomatic Myocardial Infarction: An Estimate of Its Incidence in the Living Population. H. A. Lindberg,* D. M. Berkson, J. Stamler, and A. Poindexter. Arch. Int. Med. 106:628 (Nov.) 1960. (*Department of Medicine, Heart Disease Control Program, Northwestern University School of Medicine, 303 E. Chicago Ave., Chicago, Ill.)

Among 756 men, 50 to 59 years of age, employed by a utility corporation, routine voluntary medical review revealed 20 with definite myocardial infarction (significant Q waves in the ECG of men whose earlier tracings were devoid of this finding). In four instances, the change was noted for the first time in the course of the periodic medical review. One of the four had a previously unexplained episode of dyspnea a few weeks prior to examination. The other three had no history of any cardiovascular difficulties. These data suggest that as many as 15% of myocardial infarctions may be detected for the first time by routine electrocardiography. —L.W.

Live Poliovirus Vaccine. Leading Articles, Lancet I: 1057 (May 14) 1960.

There is intense interest in attenuated poliomyelitis virus vaccines: killed vaccine though highly effective is not 100% so. As a result, frequent boosters are required, it is difficult to persuade people to be vaccinated, and it is expensive. It is believed that living attenuated vaccine will overcome these difficulties, but this must be proved. Although many millions of people have been given the vaccine without recorded ill effects, its safety and effectiveness have not been proved. Doubts about its safety revolve about the strains excreted by those vaccinated, for excreted virus can spread to others. It is feared that the virus could produce a mutant which if excreted could cause an epidemic disease.

"Further investigation is still required on several important points: the antigenic effectiveness at different ages and with different dosages; using the viruses singly or in combination; the persistence of antibody response; and the stability of the genetic characters of the virus excreted by those vaccinated."

Killed vaccine has proven its effectiveness and at present is the method of choice. A more energetic program of vaccination is needed, for there is a definite need for better prevention, be it by attenuated living virus or by a more potent killed virus possibly combined with diphtheria, whooping cough, and tetanus immunizing agents.—S.H.S.

Induced Sputum as a Diagnostic Technique for Cancer of the Lungs. A. L. Barach,* H. A. Bickerman, G. J. Beck, K. G. S. Nanda, and E. R. Pons, Jr. Arch. Int. Med. 106:230 (Aug.) 1960. (*929 Park Ave., New York 28.)

The authors have found that an increased rate of nebulization of hypertonic glycol-saline solutions is more effective than previously described methods as an adjunct in the production of sputum specimens for cytologic studies. The method is simple, safe, and acceptable to the patient.—L.W.

Meprobamate Overdosage. M. J. Ferguson,* S. Germanos, and W. J. Grace. Arch. Int. Med. 106: 237 (Aug.) 1960. (*Department of Internal Medicine, University Hospital, State University of Iowa, Iowa City.)

Meprobamate intoxication is characterized primarily by hypotension. The response to painful stimuli, the deep tendon reflexes, etc., cannot be relied upon as a guide to the patient's condition. The five cases studied were the result of massive dosage in suicidal attempts. Analeptic drugs are relatively unimportant in therapy. Vasopressor drugs and infusions as needed to control blood pressure are indicated. —L.W.

About the Authors

► ROBERT P. SIM, M.D., graduated from Columbia University College of Physicians and Surgeons in 1934. After three years of internship and a residency training, he returned to Columbia University, where he held a fellowship in Industrial Hygiene.

In July, 1938, Dr. Sim started work with the Standard Oil Company of New Jersey. Early in 1939, he was given the responsibility of developing an industrial medical program for the Company's marketing employees up and down the eastern seaboard. This work was interrupted in 1943 for active duty with the United States Navy as a lieutenant commander in the Medical Corps. After three years, he resumed the development of the Company's marketing medical services, now working from Maine to Louisiana.

In 1951, Dr. Sim went to the Columbia University School of Public Health, receiving the degree of Master of Public Health. He was certified in Public Health by the American Board of Preventive Medicine in 1952. He subsequently became Assistant Medical Director of the Esso Standard Oil Company, with supervision of seven full-time doctors in the marketing organization. He is senior author of the article in this issue, "Physical Fitness and Motor Vehicle Accidents."

► THOMAS L. SHIPMAN, M.D., was born in Andover, Mass. He received his bachelor's degree from Yale College in 1928 and his M.D. degree from Harvard Medical School in 1932. From 1936 to 1948 he was Works Physician for the Lynn, Mass., Plants of the General Electric Company. During this time he served as a Clinical Instructor in Occupational Medicine at Harvard School of Public Health. In 1948 he accepted the position of Health Division Leader at the Los Alamos Scientific Laboratory, the position he still holds.

DR. SHIPMAN is a Fellow of the Industrial Medical Association, a Fellow of the American Academy of Occupational Medicine, and is certified by the American Board of Preventive Medicine in the specialty of occupational medicine. He was a Director of the American Industrial Hygiene Association from 1950 to 1953. He currently serves as one of the representatives of the Industrial Medical Association on the National Committee on Radiation Protection and Measurements.

As senior author of the treatise entitled "Acute Radiation Death Resulting from an Accidental Nuclear Excursion," which is published as a special supplement in this issue, DR. SHIPMAN wrote the introduction, the summary, and two of the other eight sections. Authors of other sections in this supplement include:

C. C. LUSHBAUGH, M.D., whose main fields of research and practice involve pathologic histoanatomy, clinical pathologic diagnosis, medicolegal problems in pathology, cancer detection (cytologic and chemical), damage from ionizing radiation, and chemical toxicology and diagnostic radiosiotopology. He received three degrees from the University of Chicago—a B.S. in anatomy in 1938, a Ph.D. in pathology in 1942, and an M.D. in 1948. He joined the staff of the Biomedical Research Group of the Los Alamos Scientific Laboratory in the spring of 1949. He is a member of the American Association for the Advancement of Science, American Association for Cancer Research, American Medical Association, American Society for Experimental Pathology, Radiation Research Society, and the Society for Experimental Biology and Medicine.

DONALD F. PETERSEN, Ph.D., whose main fields of research include the influence of ionizing radiations on enzymatic processes in mammalian cells, analytical biochemistry, metabolism of chemotherapeutic agents, and isotopically labeled metabolites. He received his bachelor's degree in zoology from Depauw University in 1947, his master's degree in zoology from South Dakota State College in 1951, and his Ph.D. degree in pharmacology from the University of Chicago in 1954. He continued as a Research Associate in the U.S. Air Force Radiation Laboratory at the University of Chicago until going to the Los Alamos Scientific Laboratory in the fall of 1956. He is a member of the American Society of Pharmacology and Experimental Therapeutics, Radiation Research Society, American Industrial Hygiene Association, New York Academy of Sciences, and American Association for the Advancement of Science.

WRIGHT H. LANGHAM, Ph.D., whose major interests are in the fields of physiology and toxicology of plutonium, tritium, and other radioactive materials, effects of massive doses of radiation on animals, relative biological effectiveness of radiations of different types and different energies, potential hazards of world-wide radioactive fallout from nuclear weapon tests, and use of radioisotopes in biology and medicine. He received his bachelor's degree in chemistry from the Panhandle A. & M. College (Goodwell, Okla.) in 1934, and his master's degree in chemistry from Oklahoma A. & M. College (Stillwater) the following year. He studied organic chemistry at Iowa State College from 1937 to 1938, and received the degree of Ph.D. in chemistry from the University of Colorado in 1943. Immediately after this he became associated with the atomic energy program, spending a year at the Metallurgical Laboratory of the University of Chicago. In 1944 he went to Los Alamos, and late that year his interests were turned to problems of toxicology, biophysics, and health through developing methods of diagnosing exposure of Los Alamos personnel to plutonium. He became the Group Leader of the Biomedical Research Group of the Los Alamos Scientific Laboratory in 1946 and still holds that position. He is a member of the International Subcommittee on Internal Hazards of Radiation, the National Committee for Radiation Protection, the Weapons Effects Board of the Defense Atomic Support Agency, and the National Subcommittee on Incineration of Radioactive Wastes. He is also a member of the Board

About the Authors

of Directors of the Health Physics and Radiation Research Societies.

PAYNE S. HARRIS, M.D., whose major fields of interest include the physics and the effects of nuclear weapons and the biological effects of radiation. He has done specific research in dosimetry both at weapons tests and in the laboratory. He graduated from the University of Illinois in 1942 with a B.S. degree in physics. He continued in research in physics through 1942 and 1943 and then entered the University of Illinois College of Medicine, receiving his M.D. degree in 1946. He was an officer in the Medical Corps of the U.S. Army from 1947 to 1954; he taught in the Army Medical Services Graduate School from 1947 to 1949 and was assigned to duty at the Los Alamos Scientific Laboratory from 1949 to 1953. He remained in the Army one additional year and in 1954 became a permanent staff member of the Biomedical Research Group at the Los Alamos Scientific Laboratory. In 1961 he became Group Leader of the Radiation Field Studies Group in the Laboratory's Health Division. He is a consultant to the Atomic Bomb Casualty Commission, and since 1957 has been a member of the Aeromedical Panel of the U.S. Air Force Scientific Advisory Board.

JAMES N. P. LAWRENCE, whose work has been in all aspects of health physics. He has been particularly interested in applications of high-speed computers to a variety of health physics problems. He received his A.B. degree in physics at The Johns Hopkins University in 1950. The following year he was an AEC Fellow in Health Physics at the Oak Ridge National Laboratory and Vanderbilt University. He went to the Los Alamos Scientific Laboratory in 1951 and is now a Senior Health Physicist in the Health Physics Group. He received his M.A. degree from Vanderbilt in 1958.

—EDITOR

Hawaiian Tour — Last Call

There is still time to make reservations for the American Industrial Health Post-Conference tour to Hawaii, April 14-23, *but* action must be taken promptly. Ample plane and ship space is still available but must be released soon if not reserved. The tour itinerary and scientific program were published in the January, 1961, issue of this journal, page 17a. To make reservations, write promptly to International Travel Service, Palmer House, Chicago 3, Ill.

Directory of Advertisers

Aloe, A. S., Company ..... *3rd cover*
Best Foods *11a*
Ballard, E. D. Co. *16a*
Dennis, Joseph K., Co. *19a*
Eaton Laboratories *7a*
Industrial Acoustics Co. *1a*
Lilly, Eli, & Co. ..... *4th cover*
Midwest Hospital & Surgical Supply Co. *18a*
Parke, Davis & Co. *2a*
Pitman-Moore Co. ..... *2nd cover*
Robins, A. H., Co. *15a*
Vitamins-for-Industry, Inc. *13a*
Wallace Laboratories *4a-5a*

1. Everest and Jennings Wheel Chairs

2. Hollywood Wheel Chairs

Hollywood Wheel Chairs are attractive, comfortable and easy to propel. They give freedom of movement in confined spaces and fold easily for car transportation. No other chair offers so many "expensive chair" features at such low cost.

Detachable Footrests.

Both standard footrests and elevating legrests are detachable and interchangeable. No nuts or bolts involved. Simple Snap Lock permits detaching or replacing in seconds without tools. Such easy removal of these units permits close head-on approach to bed or tub.

Complete catalog on various types available upon request.

MIDWEST HOSPITAL & SURGICAL SUPPLY CO.

Chicago (21) Phones HU 3-2066-67 7209 So. Halsted St. Illinois

People and Events

► THOMAS S. ELY, M.D., has been appointed Chief, Health Protection Branch, Office of Health and Safety, U.S. Atomic Energy Commission, Washington, D. C. He had been Assistant Chief of the Branch since its formation under the Division of Biology and Medicine in 1957.

DR. ELY graduated from Bethany College, Bethany, West Virginia, in 1944 and received his M.D. degree from Georgetown University Medical School in 1948. He served his internship at the U.S. Naval Hospital, Bethesda, Md. He spent the next three years as Project Officer in the Atomic Medicine Division, Naval Medical Research Institute. From 1952 to 1954 he served as Assistant Medical Officer aboard the aircraft carrier, *U.S.S. Kearsarge*. He then returned to the Naval Medical Research Institute and was assigned to the Biophysics Division. He joined the Atomic Energy Commission in 1956 and for a year was Assistant Chief of the Medical Branch of the Division of Biology and Medicine.

He is a member of the Industrial Medical Association and serves this journal as head of the group of literature abstracters in the field of radiation health. He is also a member of the American Association for the Advancement of Science, American Radio Relay League, and the American Academy of Occupational Medicine.

► KENDALL A. ELSOM, M.D., has been named to the newly-created position of Medical Director of Scott Paper Company. He will be located at the company's headquarters in Chester, Pa. In his new post, he will serve as liaison with physicians retained at all Scott plants and will be responsible for all phases of the company's industrial health program.

Since 1951 DR. ELSOM has been Director of the Diagnostic Clinic at the Hospital of the University of Pennsylvania. He will maintain his association with the University Hospital where he will continue a research project involving health examinations for executive personnel.

Thomas S. Ely, M.D.

DR. ELSOM was graduated in 1924 from the University of Wisconsin where he served for a year as student instructor in physiology. He then entered the University of Pennsylvania and was awarded his M.D. degree in 1927. After serving his internship in the University's Graduate Hospital, he held appointments in the Departments of Pharmacology and Medicine.

During World War II, DR. ELSOM was Chief of Gastroenterology and later Assistant Chief of Medical Service with the 20th General Hospital in Ledo, Assam, India. During his last six months of military service he was Chief of Medicine at the Army Service Forces Hospital, Fort Benning, Ga. He was discharged with the rank of lieutenant colonel. In 1947 DR. ELSOM returned to the University of Pennsylvania Hospital.

DR. ELSOM holds the rank of Professor of Clinical Medicine. He is a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, the American Gastroenterological Association, the Philadelphia College of Physicians and an emeritus member of the American Society of Clinical Investigation.

AN EXCLUSIVE PRIVILEGE OF I.M.A. MEMBERSHIP

Program No. 1

Up to $400.00 Per Month Tax Free Accident and Sickness Disability Income Benefits

Program No. 2

From $25,000.00 to $200,000.00 Worldwide Accidental Death, Dismemberment And Loss of Eyesight Indemnity

MAIL TODAY TO:

IMA Group Insurance Administration Office
Joseph K. Dennis Company, Incorporated
Suite 1027 – 175 W. Jackson Blvd.
Chicago 4, Illinois

Please send me up to date descriptive material and rates.

Name .....

Date of Birth, Member ..... Spouse .....

Address .....

City ..... State .....

People and Events

► JOHN M. BREWSTER, M.D., has been appointed Medical Director of the Pennsylvania Railroad. He will have system-wide supervision over the railroad's health maintenance program. He succeeds ALEXANDER M. W. HURSH, M.D., who is retiring.

DR. BREWSTER joined the Pennsylvania Railroad in 1952 as Medical Officer, Philadelphia Terminal Division, and has been Region Medical Officer at Philadelphia since 1955. He received his M.D. degree from Jefferson Medical College of Philadelphia in 1923 and completed a postgraduate course in surgery at the University of Pennsylvania.

Serving in the U.S. Navy medical corps, he was senior medical officer on the *U.S.S. Pennsylvania*, flagship of the Pacific fleet, when she was attacked by the Japanese at Pearl Harbor. He was commanding officer of a fleet hospital in the South Pacific during World War II, after which he continued in the Navy as fleet medical officer, executive officer of the Great Lakes Naval Hospital, commanding officer of the Corpus Christi, Tex., Naval Hospital, and senior medical member of the Fourth Naval District physical evaluation board.

DR. BREWSTER is a Fellow of the American College of Surgeons, a member of the staffs of Bryn Mawr and St. Agnes Hospitals, and a lecturer in preventive medicine at the University of Pennsylvania Medical School.

DR. HURSH, retiring Medical Director, received his pre-medical education at Dickinson College, where his studies were interrupted by service in the Army during World War I. He received his degree in medicine from Jefferson Medical College in 1923. He began railroad work in 1925 as an assistant medical examiner at Sunbury, Pa. After serving as medical examiner at several locations, he was named Chief Medical Examiner at Philadelphia in 1945, Assistant Medical Director in 1953 and Medical Director in 1958. He is a member of the executive committee of the American Association of Railway Surgeons.

► NORVIN C. KIEFER, M.D. Chief Medical Director of Equitable Life Assurance Society of the U.S., has been appointed chairman of the 1962 National Health Forum, it was announced by JAMES E. PERKINS, M.D., president of the National Health Council, which sponsors the annual health forums. The subject of the 1962 Forum will be "Accident Prevention and Emergency Care." It will be held in Cleveland, Ohio, the week of March 19-23, and will bring together leaders from the fields of health, industry, organized labor, farming, science, safety engineering, insurance, education and government to discuss chronic problems of accident prevention and emergency care and what can and must be done about them.

DR. KIEFER is now serving his fifth term as president of the Greater New York Safety Council and is a member of the board of the National Safety Council. From 1958 to 1959, he was president of the National Health Council and is a member of its board.

► New York State Society of Industrial Medicine will hold a luncheon meeting on March 29 at the New York University Club. IRVING TABERSHAW, M.D., Scientific Director, J. E. Seagrams & Sons, Inc., will speak on "The Role of Drugs in Occupational Medicine."

► Kentucky Industrial Medical Association will meet March 23 at the plant of the General Electric Company, Appliance Park, Louisville. A plant tour will precede the meeting at which CHARLES F. MARTIN, M.D., President-Elect of KIMA, will preside. DR. MARTIN is Plant Medical Director of International Business Machines at Lexington, Ky.

The program will feature a panel discussion on the subject, "When Should My Patient Return to Work?" Moderator will be W. E. POWLES, M.D., of the University of Cincinnati College of Medicine. Panel members and their specific subjects are as follows: "The Sore Back Returns to Work"—KERNS R. THOMPSON, M.D., Lexington, Ky.; "The Occupational Physician Views the Patient Returning to Work"—RICHARD C. SWAN, M.D., Medical Director, Delco Remy Division, Anderson, Ind.; "The Cardiac Returns to Work"—C. ANTHONY D'ALONZO, M.D., Assistant Medical Director, E. I. du Pont de Nemours & Co., Wilmington, Del.

An after-dinner address will be presented by JOE M. BOSWORTH, M.D., Regional Medical Director, Liberty Mutual Insurance Company, Atlanta, Ga. His subject will be "What Industrial Medicine Has to Offer the Employee."

► Michigan Industrial Medical Association will hold its annual meeting at the Statler Hilton Hotel in Detroit on March 24. DUANE L. BLOCK, M.D., President, will preside at the morning session which will include a presentation entitled "Acute Psychiatric Problems in Industry" by MARVIN SHERMAN, M.D., Psychiatrist, Metropolitan Hospital, Detroit, and a panel discussion on the subject "Problems of the Aging Worker." Panel members HAZEN PRICE, M.D., Internist; L. J. LANGTON, Industrial Engineer; and LOUIS STEINER, M.D., Internist, Henry Ford Hospital, Detroit, will discuss the problem as viewed by the private physician, the industrial engineer, and the disability examiner, respectively.

RICHARD MUDD, M.D., President-Elect, will preside over the afternoon session which will include the following scientific presentations: "Closed Chest Cardiac Massage"—MUIR CLAPPER, M.D., Associate Professor of Medicine, Wayne State University; "Acute Renal Failure"—IVAN J. MADER, M.D., Internist, Detroit Receiving Hospital; "Petroleum Products and Carcinogenesis"—ROBERT E. ECKARDT, M.D., Medical Director, Esso Research and Engineering Company, Linden, N.J.

W. HARTSELL WILSON, Assistant General Sales Manager, Plymouth Division, Chrysler Corporation, will speak at the annual dinner.

► Industrial Medical Association of Philadelphia will hold its annual joint meeting with the Philadelphia Section of the American Industrial Hygiene Association at the Engineers' Club on March 15. LUCIEN A. BROUHA, M.D., an authority on the effects of environment on health and productivity will speak on "Environmental Stress." DR. BROUHA is with the Haskell Laboratory of Industrial Medical Research, E. I. du Pont de Nemours & Co., Wilmington, Del.

Journal of Occupational Medicine

SPECIAL SUPPLEMENT

MARCH, 1961

Acute Radiation Death Resulting from an Accidental Nuclear Critical Excursion

From the Los Alamos Scientific Laboratory, University of California, Los Alamos, New Mexico. This work was done under the auspices of the U.S. Atomic Energy Commission.

	Introduction	*Thomas L. Shipman, M.D.*	146
I.	Description of the Accident and Subsequent Events	*Thomas L. Shipman, M.D.*	147
II.	Clinical Course of Case K	*C. C. Lushbaugh, M.D.*	150
III.	Clinical Pathology and Biochemistry	*Donald F. Petersen, Ph.D.*	155
IV.	Gross and Microscopic Pathology and Neuropathology	*C. C. Lushbaugh, M.D.*	160
V.	Special Studies	*Wright H. Langham, Ph.D.*	169
VI.	Dosimetric Calculations	*Payne S. Harris, M.D.*	178
VII.	Health Physics Studies and Area Radiation Levels	*James N. P. Lawrence, M.A.*	184
VIII.	Report on Other Personnel Exposed	*Thomas L. Shipman, M.D.*	188
IX.	Summary	*Thomas L. Shipman, M.D.*	191

Introduction

ANY ACCIDENT involving radiation or radioactivity is of interest to scientists and the general public because of the recognized need for knowledge of the hazards associated with nuclear operations. A situation in which humans receive excessive exposure to ionizing radiation is justifiably a matter of intense interest to physicians, biochemists, pathologists, and others who are concerned with studies of the physical phenomena associated with acute radiation illness. It is also of great concern to physicists and health physicists who are charged with the development of systems and procedures to ensure the safety of operations involving active material, since in ordinary laboratory operations risks of any degree are unacceptable.

As far as is known, all previous radiation accidents resulting in acute lethality have been described in the literature. Hempelmann et al.[1] discussed two such cases occurring in 1945 and 1946, and Jammet[2] and Mathe[3] have described a more recent one. Other papers[4–6] have given additional accounts of accidents which caused no fatalities, but which easily could have done so save for fortuitous circumstances.

The accident to be discussed in the following pages occurred at the Los Alamos Scientific Laboratory on the afternoon of Dec. 30, 1958, and it is of interest because it involves the largest accidental dose of radiation yet received by a human. If a single case can be accepted as significant, it completes the triad of the three modalities of acute lethality in humans resulting from ionizing radiation.

Since the technical data relative to the chemistry and physics of the accident are given in the official report by Paxton et al.[7] and in a shorter paper by the same authors,[8] they are not included in this monograph, the purpose of which is to present the medical aspects of the cases involved to promote better understanding of the nature of radiation injury.

The sections are by different authors who discuss those facets of the case with which they are most familiar. There are some areas of repetition, since each author was encouraged to include all details pertinent to his presentation.

None of the discussions represent the work of the authors alone; many individuals collaborated and contributed much vital material. A complete list of acknowledgments would cover much of the Health Division of the Los Alamos Scientific Laboratory, many individuals in other Divisions, the Los Alamos Medical Center, and a number of valued colleagues in other parts of the country. Some of these are mentioned by name; all of them deserve our thanks.

—THOMAS L. SHIPMAN, M.D.
Health Division Leader
Los Alamos Scientific Laboratory

SECTION I

Description of the Accident and Subsequent Events

Thomas L. Shipman, M.D.

AT 4:35 P.M. on Dec. 30, 1958, an accidental critical excursion resulting in fatal radiation injury to an employee took place in the plutonium recovery plant at DP West Site of the Los Alamos Scientific Laboratory. The time is significant because 10 or 15 minutes earlier the room had been occupied by perhaps a half-dozen maintenance workers, whose shift ended at 4:30; and the date is important because, when the accident occurred, a year-end physical inventory of fissionable material was being conducted, and normal flow of material into the system was interrupted.

The accident occurred in an area in which "lean" residues of waste material, usually in solutions containing less than 0.1 gm Pu/liter, were processed for recovery of the plutonium. This was a routine operation, one that had been carried out many times over a number of years, and it was implicit in the system and operating procedures that the tanks used in the process could not contain enough plutonium at any one time to permit a critical reaction.

Reconstruction of events that preceded the excursion indicates that plutonium-rich solids that normally would have been handled separately were washed from two tanks into a large vessel that contained dilute aqueous and organic solutions. Most of the aqueous solution was removed from this vessel; then the remaining 40 gal. of material was transferred to a stainless steel solvent-treating tank which already contained about 80 gal. of emulsion that had resulted from another step in the recovery process.

Fig. 1 shows the solvent-treating tank and the assumed position of chemical operator K* just prior to the accident. He stood on the short stepladder shown in the photograph, looked

* With the exception of K, the victim of the accident, the individuals involved are designated by randomly selected letters of the alphabet.

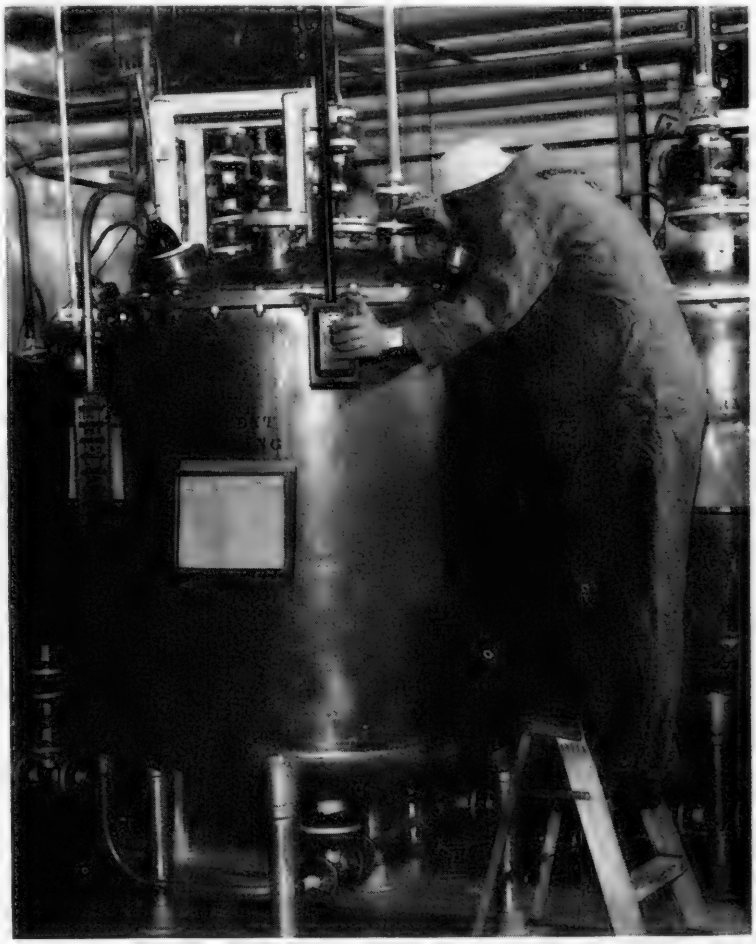


Fig. 1—The tank in which the critical excursion took place and the assumed position of the victim of the accident, K.

through the viewport into the tank, and with his left hand pressed the switch to start the motor for the propeller-type stirrer inside the tank. This is further described in Section VI. It was the normal procedure and was subsequently reenacted by a number of individuals. Almost immediately the critical reaction took place. K either fell or was knocked to the floor. He evidently turned the stirrer motor off and on again, then ran to the door leading outside the building. His motivation for this is unknown, but he was apparently confused and disoriented.

Fig. 2 shows the floor layout. The circles indicate steel tanks of varying sizes. From this and Fig. 1, it can be seen that the room was a maze of tanks and pipes. Fig. 1 also shows that an emergency shower existed immediately beside the tank in which the critical reaction took place.

Two chemical operators, D and R, were in the immediate vicinity of the critical excursion innocently triggered by K. D was at his work position some 40 ft. away, carrying out another phase of the recovery operation. It can be seen from Fig. 2 that he was well shielded by a wall and a series of tanks. His back was toward Room 218, but he was alerted by the reflection of a bright light on the wall he faced, together with a noise he described as a dull thud. The light was certainly not the "blue glow" mentioned in connection with other radiation accidents; D described it as being like the light from a photoflash bulb or a short circuit. His feeling was that there had been an electrical accident of some sort, and it is possible that the intense radiation field had actually caused arcing in the motor of the stirrer on top of the tank.

Feeling something had gone wrong, D went to help and was joined by R. By this time, K was outdoors, and he was even now ataxic and disoriented. All he could say was, "I'm burning up, I'm burning up!"

Since this was a chemical operation involving large quantities of acids and caustics, D understandably assumed that there had been a chemical accident; so he and R led K to a shower, returning past the accident tank, where D stopped the motor to the stirrer. They knew there was a shower beside K's work station, but both were trained and experienced in work with plutonium. Considering the possibility of alpha contamination, they continued to the more distant shower near the exit from Room 213.

By this time K could not stand unaided; so after he was showered the two other men placed him on the floor of an adjacent airlock, where he lay essentially unconscious. R went to summon assistance, and D returned to Room 218 to see whether the system was properly shut down. He spent one or two minutes in the room, and undoubtedly passed several times within 2 or 3 ft. of the tank, which was still intensely radioactive. Finding nothing out of order, he returned to the airlock.

Since a critical excursion in the plutonium-

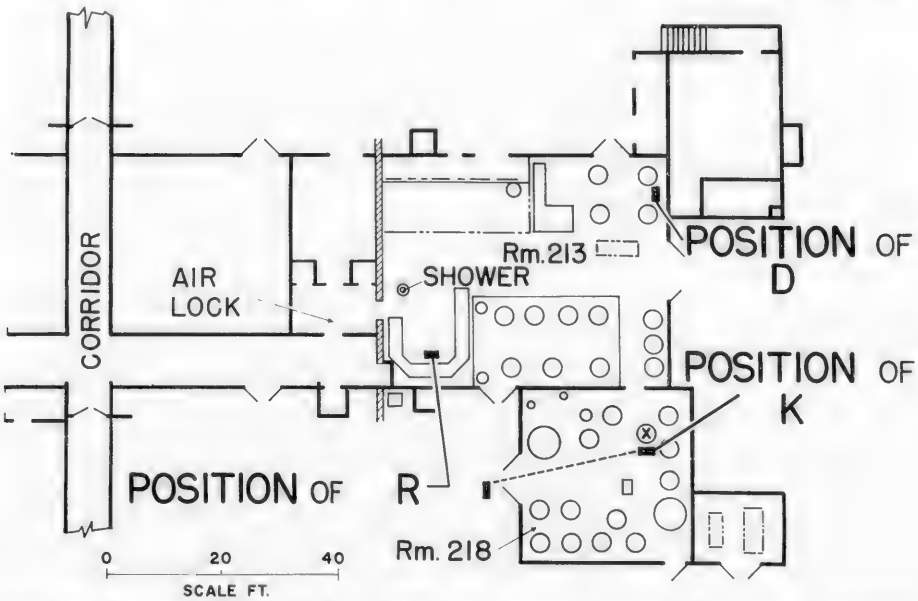


Fig. 2—Floor plan of rooms 213-218 DP West where the accident occurred. The circles represent chemical treatment tanks, and the one marked with an X is that shown in Fig. 1.

recovery system had been considered inconceivable, there were no gamma-sensing detectors in the immediate area.† The burst activated a radiation alarm 175 ft. away in a nearby building, but the workers in that area, finding no sign of trouble, assumed it had sounded accidentally and resumed work.

Between 4:40 and 4:45 p.m., 5 to 10 minutes after the accident, supervisors and monitoring staff converged on the area in answer to R's call for help. They found no widespread alpha activity (considered the principal problem), and it was not until 4:52 p.m. that the area monitoring supervisor first detected the presence of gamma activity. With its discovery, the entire area was evacuated.

The nurse stationed in the area arrived at the airlock at 4:46 p.m., at which time the ambulance was summoned. She made the very pertinent observation (although its significance was not apparent at the moment) that K obviously was in shock and virtually unconscious but "with a nice pink skin." This, of course, was the erythema, already evident. The ambulance and patient left for the hospital at approximately 4:53 p.m.

† As a result of a nuclear-safety survey conducted about a month before the accident, gamma-radiation alarms had been ordered for the entire plutonium facility as an additional precaution, but they had not yet been installed.

K arrived at the hospital with neither a diagnosis nor a history that would lead to a diagnosis. He was admitted simply as a patient virtually unconscious and in shock. He was so close to death at the time of admission, however, that his early treatment would unquestionably have been the same had the nature of the accident been clear from the beginning.

At the scene of the accident, the situation was now reasonably clear. At 4:52 p.m. the gamma level at the north door of Room 218, the door leading outside, was recorded as 20 r/hr. At 5:10 p.m. the level at the east door, leading from the room where D had been at work, was 45 r/hr.

Precise calculation of the doses received by the victims of the accident required much time, but it was apparent within perhaps two hours that K had almost certainly received a massive supralethal dose of several thousand rads, and that D and R had received doses that were significant but far below lethality. In order to make the discussions that follow more understandable, the final figures are given here. K's dose varied from approximately 12,000 rads to the upper abdomen to less than 100 rads to the lower extremities. This might be averaged to approximately 4,500 rads of whole-body radiation. D's dose was approximately 130 rads, and that of R was about 35 rads. All these figures include dosage from neutrons and gamma rays.

SECTION II

Clinical Course of Case K

C. C. Lushbaugh, M.D.
With the collaboration of Robert S. Grier, M.D., John S. Benson, M.D., and Donald F. Petersen, Ph.D.

IN RETROSPECT, the clinical course of patient K can be divided into four rather distinct periods, differing in duration, symptomatology, and response to supportive therapy. The first period (lasting about 20 to 30 minutes) was characterized by his immediate physical collapse and mental incapacitation, which progressed to semiconsciousness and severe prostration (see Section I). The second period (lasting about one and one-half hours) began with his arrival by stretcher at the emergency room of the hospital and ended with his transfer from the emergency room to the ward for further supportive therapy. This second period was characterized by such severe cardiovascular shock that death seemed imminent during the whole time. During this period he seemed to be suffering severe abdominal pain. The third period was about 28 hours in length and was characterized by enough subjective improvement to encourage continued attempts to alleviate his anoxia, hypotension, and circulatory failure. The fourth period began with the unheralded onset of rapidly increasing irritability and uncooperativeness, bordering on mania, followed by coma and death in approximately two hours. The entire clinical course lasted 35 hours from the time of radiation exposure to death.

When the patient was seen first in the Los Alamos Medical Center emergency room, he was semiconscious and incoherent, retching, vomiting, and hyperventilating. His skin was cold, dusky reddish-violet, and his lips and oral mucous membranes were extremely cyanotic. The conjunctivae were so hyperemic that they appeared to have been injured by a welder's arc. He was immediately wrapped in warmed blankets and surrounded by hot water bottles. His blood pressure and radial pulse were at first unobtainable, but his apical heart rate was 160 per minute (just audible by stethoscope). His lungs seemed to be clear to auscultation. He had shaking chills and coarse purposeless movements of his extremities and torso, which necessitated restraint by the nursing staff.

About 10 minutes after arrival in the emergency room, he had an attack of propulsive, watery diarrhea which contained some large well-formed stools (later radioassayed, see Section V). At this time his blood pressure was successfully determined at 80/40 and his pulse rate as 160 per minute. A 30 ml sample of blood was obtained for laboratory and dosimetric measurements (see Sections V and VI). External monitoring with a portable survey instrument showed a body surface gamma-ray reading of 15 mr/hr. His feces and vomitus at this time were also sufficiently radioactive to give a demonstrable gamma-ray reading on the survey instrument.

He was given 25 mg of Thorazine, 0.4 mg of atropine, and 60 mg of sodium luminal, but his extreme anxiety and restlessness were not resolved until after receiving 50 mg of Demerol parenterally. An intravenous infusion of 5% dextrose in physiologic saline containing 20 ml of 10% calcium gluconate was started with the intention that this fluid would be replaced by blood just as soon as a cross-match could be completed. The calcium gluconate appeared to be responsible for cessation of his widespread muscular tremors. The clinical impression of profound shock was supported by laboratory findings of an 18 gm hemoglobin and a 58% hematocrit (Fig. 3). The first cross-match was rejected because of positive Coombs' reactions in both major and minor fields, and blood transfusion was deferred until additional cross-matches could be performed. Whole blood, however, was never given because, as shown in Fig. 3, he developed no anemia, and after the first six hours he had relatively stable hemoglobin and hematocrit values. The additional cross-

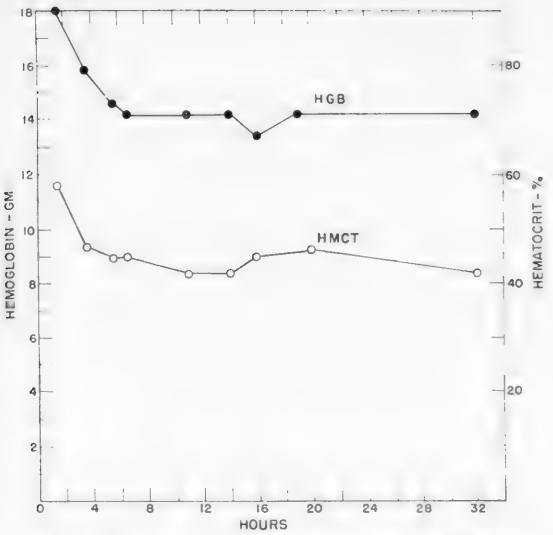


Fig. 3—Changes in hemoglobin and hematocrit following exposure (Case K).

matching continued to be complicated by positive Coombs' reactions with both his serum and his cells. This finding was explained later, when it was found that his own cells were agglutinated by Coombs' serum in the absence of foreign plasma, indicating the presence of isoantibodies on his own cells and free in his serum. This explanation then allowed the use of plasma in the treatment of his shock. More definitive studies of the nature of his antibody and serum proteins were made later (see Section III). Five determinations of his serum bilirubin over the first 25 hours failed to show a significant rise in either the direct or the indirect reaction, suggesting that hemolysis, if any, was negligible.

As coherence slowly returned to the patient, he complained of severe abdominal cramps, but neither increased nor abnormal bowel sounds could be heard. Although nausea continued and he occasionally retched and vomited, he seemed considerably improved. He was transferred to a room, where 1 hour and 40 minutes after the accident (6:16 p.m.) he was placed in bed on shock blocks and in an oxygen tent. Preliminary reports from the radioassays of the first blood sample estimated that his total exposure had been massive and probably supralethal.

As soon as he was resting quietly, he was examined thoroughly. The only positive finding, other than his continuing hypotension (85/45), tachycardia (140), and intense dermal and conjunctival hyperemia, was a temperature of 103°F rectally (Fig. 4). The examination revealed normal ocular fundi, normal cranial and peripheral nerves, normal but cyanotic mucous membranes, clear lungs, and sore abdominal muscles. Both hands and forearms seemed swollen. Although his erythema was most intense over the anterior surface of his face, thorax, abdomen, genitalia, and upper half of the thighs, its full extent was not delineated because it extended posteriorly and inferiorly without sharp borders. He complained of his mouth being dry but was not allowed to drink until several hours later. Forty milligrams of vasopressor amine* was added to his infusion without appreciably improving his blood pressure (Fig. 5). Fig. 5 also shows the relationship between the patient's systolic blood pressure, measurable fluid losses, accumulated

* Wyamine and Levophed were used.

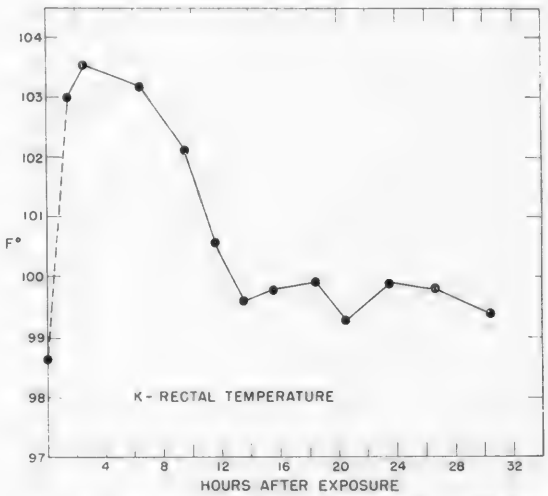


Fig. 4—Changes in rectal temperature following exposure (Case K).

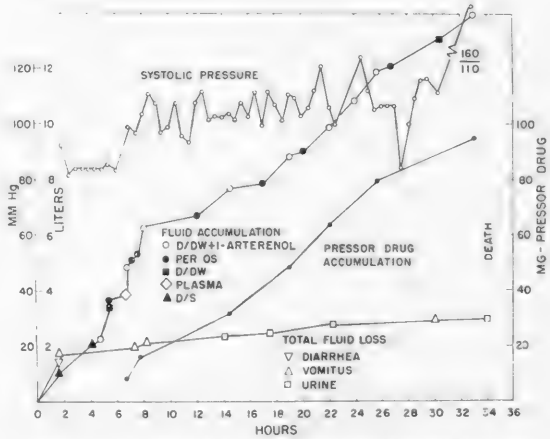


Fig. 5—Composite graph of systolic blood pressure, amount of fluid and vasopressor (levarterenol) administered, and amount of fluid lost via oral, urinary, and fecal routes.

Table I—Summary of Therapeutic Agents Employed in the Symptomatic Treatment of Case K

Compound*	Dose	Doses Administered	Rationale
Atropine	0.4 mg	1	Intestinal hypermotility
Thorazine	25 mg	1	Apprehension
Phenobarbital	120 mg	7	Irritability and insomnia
Hydeltrasol (prednisolone)	20 mg	6	Adrenal cortical failure (?)
Calcium gluconate	20 ml	1	Muscular tremors
B complex	5 ml	1	Coenzyme depletion
Demerol (meperidine)	50 mg	4	Epigastric pain
Wyamine (mephentermine)	7.5 mg	3	Hypotension
Aramine (metaraminol)	30 mg	2	Hypotension
Levophed (levarterenol)	8 mg	6	Hypotension
Compazine (perchlorpromazine)	5 mg	1	Apprehension
Regitine (phentolamine)	5 mg	1	Vascular spasm
Alidase (hyaluronidase)	150 units	1	Local edema
Sparine (promazine)	100 mg	1	Apprehension
Morphine	10 mg	2	Pain and irritability
Nalline	10 mg	1	Morphine antagonism

* Arranged in order of first administration.

fluids, and accumulated amounts of vasopressor substances administered during the entire course of the disease. The abrupt declines in systolic pressure seemed to occur when the rate of flow of the infusion was decreased. Failure of the hemoglobin and hematocrit to decline with progressive fluid administration was difficult to interpret at the time and, in fact, encouraged continuation of his fluid therapy. A number of other medications were used in the attempt to control K's clinical course. A complete summary of the therapeutic agents employed in the symptomatic management of the patient is shown in Table I, where the specific drugs are tabulated in order of their first use, together with the rationale.

K's rectal temperature varied between 103 and 103.5°F for the first six hours and then fell precipitously to normal, where it remained for the duration of his life (Fig. 4). This high initial temperature and its maintenance for six hours were considered in keeping with his suspected massive dose of radiation and were considered to be prognostically grave.[1, 6] Three hours after exposure he was resting quietly, but his radial pulse could still be determined only with difficulty and cyanosis developed whenever he was taken out of the oxygen tent. An electrocardiogram taken approximately 18 hours after exposure (Fig. 6) showed a sinus tachycardia (110/min) and findings consistent with electrical preponderance of the left ventricle. In retrospect (see Section IV, paragraphs on myocardial pathology), these findings were probably best explained as being due to decreased electrical contribution from the right ventricle, resulting in apparent left ventricular preponderance.

The patient was unable to void until 14 hours after the accident (Fig. 5). The results obtained by clinical laboratory test on the first two blood specimens (Table II) reflected this anuria, which was probably a major factor in his rising serum electrolytes, nonprotein nitro-

Table II—Changes in Serum and Urinary Constituents Following Acute Gamma-Neutron Exposure (Case K)

Hours After Exposure	Serum							Urine
	Na (mEq/l)	Cl (mEq/l)	K (mEq/l)	CO_2 cap (mEq/l)	NPN (mg %)	BUN (mg %)	Uric Acid (mg %)	Uric Acid (mg %)
1½	145	113	5.2	.....	41	13	4.8	.....
3½	148	116	5.4	.....	46	20	11.6	.....
5½	148	.....	....	.....	44	33	11.4	.....
6½	.....	.....	....	.....	48	....	16.2	.....
10½	148	.....	....	.....	53	....	17.2	.....
14	.....	.....	....	.....	54	25	.....	258
16	.....	.....	....	.....	54	....	14.4	.....
17	.....	.....	....	.....	....	....	.....	173
19	.....	.....	....	.....	62	42	11.8	.....
20	.....	.....	....	.....	51	20	16.2	.....
22	.....	.....	....	.....	....	....	.....	135
25	143	199	5.1	15	68	43	.....	.....
Normal range	135-145	99-108	3.5-5	22-30	25-30	10-15	2-5	10-200

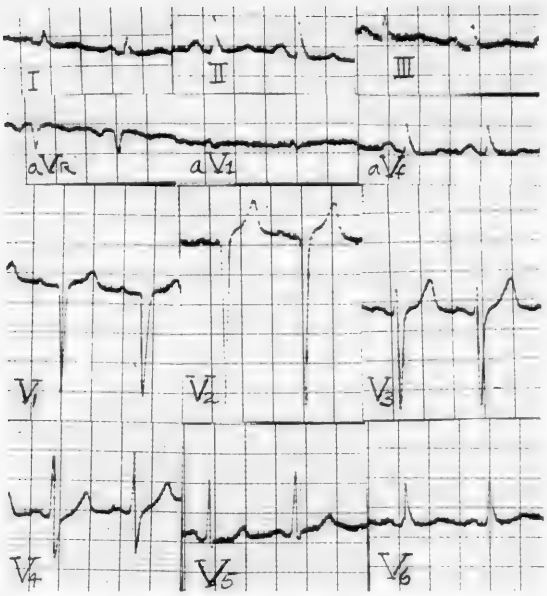


Fig. 6—Electrocardiographic study made about 18 hours after exposure (Case K). Description: Sinus tachycardia. Rate, 110 per minute. PR interval, 0.16 second. QRS duration, 0.09 second. Q-T interval, 0.32 second. Mean QRS axis, plus 60° with transition at V_4. Mean T axis, plus 60°, with T waves upright V_1 through V_6. Absent R wave at V_1 and rudimentary R wave at V_2 with a prominent S wave at V_2.

Impression: Borderline record due to QRS configuration at V_1 and V_2. Rudimentary R waves with a prominent S wave at V_2 may be associated with electrical position or left ventricular hypertrophy or occasionally as residual evidence of anterior wall myocardial infarction. Excluding electrical position, this finding is consistent with electrical preponderance of the left ventricle as commonly seen in anterior infarction or left ventricular hypertrophy. In this case, the electrocardiographic findings are not diagnostic but are consistent with decreased electrical contribution from the right ventricle, resulting in apparent left ventricular preponderance.

gen, blood urea nitrogen, and serum uric acid. (See Section IV, where necropsy findings of early widespread hematologic cell death indicated that much of this rise was a prerenal azotemia.)

A total of 10 blood samples and 3 urine specimens were obtained for diagnostic and radiobiological studies. The results of those studies which contributed to K's medical care are given in Table II. These results showed severe nitrogen retention and an increased production of nitrogenous waste products. When considered together with his continued hypotension, these results led to a rate of intravenous fluid administration which, in retrospect, may appear to have been excessive (Fig. 5). At the time, however, maintenance of adequate blood pressure seemed fundamental to prolongation of life and in particular to promoting renal function. In Section III, results of additional biochemical and hematological studies are tabulated and discussed.

Of all the various determinations made during the course of the illness, changes in white cell count were found to be the simplest and best prognostic indicator of severe irradiation. The virtual disappearance of lymphocytes from the peripheral circulation within six hours of exposure was considered a grave sign (Fig. 7). The clinical course of the patient's illness and associated laboratory findings (Table II), including morphologic changes, differed from those seen in heavily irradiated animals[9] only in the initial hyperpyrexia and absence of terminal hypothermia and specific late neurologic signs of central nervous system disturbance. These differences could have resulted from the supportive therapy, which the animals did not receive.

Twenty-four hours after the accident, a sternal bone marrow biopsy was performed. The marrow appeared watery rather than bloody, and no excessive bleeding occurred. Examination of smears from the marrow (and later fixed sections) showed an almost completely acellular, edematous, hemorrhagic fatty tissue. The finding, together with the rapid onset of lymphopenia, supported the conclusion that a supralethal dose had been received. Accordingly, arrangements were made to obtain as soon as possible fetal and cadaver marrow for transfusion, but the patient's early death precluded its use.

During the course of his second evening,

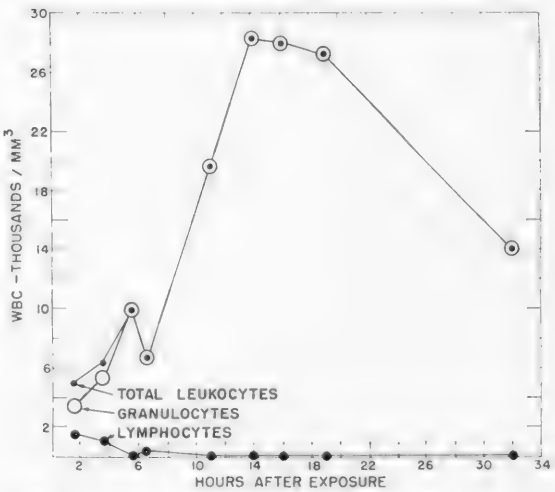


Fig. 7—Peripheral blood leukocyte changes following exposure (Case K).

difficulty was encountered in controlling pain from recurring abdominal cramps, and the patient became increasingly restless in spite of repeated doses of Demerol (50 mg) and sodium luminal (120 mg). He finally became so difficult to control that the intravenous infusions infiltrated extravascularly and were inadvertently interrupted. About 30 hours after the accident (at which time his temperature had been steady at 99.8°F for several hours), he began to sweat profusely and complained of severe diaphragmatic pain, his color became ashen and his pulse irregular. After a 45-minute interval, during which time his nurse had been unable to determine his blood pressure, it was found to be 160/110. Shortly thereafter, he began thrashing about so violently that it was difficult to keep him either in the oxygen tent or in bed, and the intravenous infusions were again disrupted. In spite of administration of oxygen by mask, his lips and nails became cyanotic and his respirations shallow. He again became incoherent and practically unmanageable about 32 hours after the accident. One hundred twenty milligrams of luminal and 10 mg of morphine given intramuscularly quieted him in about 20 minutes. Even with oxygen administration, however, his respirations became slower (18 to 20 per minute, declining slowly to less than 10 per minute) and his pulse was unobtainable. His heart tones were quite distant, slow, and irregular becoming progressively weaker and slower; they suddenly stopped 34¾ hours after the radiation exposure.

Acknowledgments

The technical assistance of Bessie Armstrong, Dorothy Hale, and Lora Belle Hughes is gratefully acknowledged, as well as aid from the Los Alamos Medical Center laboratory and nursing staffs and Los Alamos Scientific Laboratory staff. We wish also to express our appreciation to Lawrence E. Lamb, M.D., Chief of Internal Medicine and principal cardiologist at the Brooks Air Force Base School of Aviation Medicine, for aid in interpretation of the electrocardiograms.

SECTION III

Clinical Pathology and Biochemistry

Donald F. Petersen, Ph.D.
With the collaboration of C. C. Lushbaugh, M.D.

IN VIEW of the massive radiation exposure sustained by K, it was radiobiologically important to investigate a number of biochemical processes not directly related to his clinical management. In most cases, these analyses were conducted simultaneously and under identical analytical conditions with material collected from the less heavily irradiated patient D and from normal subjects. Understandably, the number of additional biochemical investigations performed in this case was severely limited by the small amount of analytical material available. Table III summarizes the details of collection and preservation of samples used in the studies described below. For the most part, significant changes in the biochemical parameters which were studied occurred only in the heavily irradiated patient, K.

Table III—Material Available from Case K for Analysis

Urine		
Voided 6:30 a.m. 12/31/58		150 ml*
Voided 10:00 a.m. 12/31/58		180 ml*
Voided 2:40 p.m. 12/31/58		260 ml*
From urinary bladder at autopsy 6:30 a.m. 1/1/59		3 ml
Feces		
Formed stool obtained in emergency room approximately 5:20 p.m. 12/30/58		36.4 gm
From diarrhea 5:25 p.m. 12/30/58		64 gm
Blood		
Serum and/or plasma†	6:10 p.m. 12/30/58	
	8:00 p.m. 12/30/58	
	10:00 p.m. 12/30/58	
	3:15 a.m. 12/31/58	
	8:30 a.m. 12/31/58	
	11:15 a.m. 12/31/58	
	12:30 p.m. 12/31/58	
	5:15 p.m. 12/31/58	
Serum obtained at autopsy	6:30 a.m. 1/1/59	
Post mortem clots		

* These samples constituted total voidings during survival time.

† All materials not used immediately were frozen and stored at −20°C in sealed containers.

Alterations in Serum Constituents Following Acute Gamma-Neutron Exposure

Serum Enzymes—Radiation-induced increases in glutamic oxalacetic transaminase (GOT) activity have been reported in sera of irradiated experimental animals and patients receiving localized roentgen therapy.[10] A notable feature of our previous studies was the rapid onset of detectable change in serum enzyme content following exposure. However, no correlation between the dose administered and the magnitude of the change could be demonstrated and, owing to rapid destruction of circulating enzyme by the hepatic parenchyma, GOT measurements were considered unsuitable as a quantitative indication of the extent of radiation injury.[11] Nevertheless, these studies did demonstrate a consistent increase in a number of serum enzymes after exposure to x-rays and gamma-neutron irradiation, and it seemed desirable, therefore, to ascertain the effect of a massive dose of gamma-neutron irradiation on serum enzyme levels in man.

Glutamic oxalacetic transaminase, glutamic pyruvic transaminase (GPT), lactic dehydrogenase (LDH), and malic dehydrogenase (MDH) assays were performed by modifications of existing methods,[12-15] based on the spectrophotometric measurement of the rate of disappearance of reduced diphosphopyridine nucleotide from the reaction mixture at 38°C. All results have been corrected for temperature to facilitate comparison with clinical data where assays are conventionally carried out at room temperature. Measurements of serum lactic and malic dehydrogenase were discontinued because of limitations in available analytical material. Results of these analyses are summarized in Table IV. K's serum GOT activity was approximately twice normal in the earliest sample obtained one and one-half hours after irradiation. Subsequent analyses showed a gradual increase to six times normal during the succeeding 23 hours. Serum GPT activity did not exceed

*Table IV—Serum Enzyme Content**

Sample	Hours After Exposure	SGOT	SGPT	LDH	MDH
Case K	1½	53	31	676	310
	3½	42	29	.....	.....
	5½	55	29	.....	.....
	10½	101	32	.....	.....
	16	55	25	.....	.....
	19	116	24	.....	.....
	25	160	37	.....	.....
	Post mortem	429	58	.....	.....
Case D	4	17	44	604	136
	17	23	38	.....	.....
Control	....	26	24	388	113
Normal range		14-35	8-30	200-600	50-104

* Assays based on disappearance of reduced diphosphopyridine nucleotide at 340 μ, 38°C, corrected to reaction rate at room temperature for comparision with conventional clinical values.

Unit = decrease in optical density of 0.001/min/ml of serum.

normal levels before death, but both enzymes exhibited characteristic postmortem increases. These data are in contrast with negative findings reported after smaller doses of radiation sustained in the Oak Ridge Y-12 accident[6] but are in agreement with our previous experience with monkeys exposed to fission neutrons.[11] K's values for serum enzyme activity were undoubtedly modified by retention of most of the large volume of intravenous fluids administered. Since it has been shown[11, 16] that these serum enzymes are in equilibrium in the total extracellular fluid space rather than in the circulating fluid volume, actual serum enzyme values were probably one-third higher than the values obtained. Serum lactic and malic dehydrogenase values were also slightly elevated in the initial serum sample in comparison with the control value determined simultaneously. No significant abnormalities in serum enzyme content attributable to radiation injury were noted in sample obtained from the second patient, D.

The hypothesis has been advanced that necrosis of irradiated cells results from destruction of proteolytic enzyme inhibitors and the subsequent action of liberated cathepsins.[17] Results of serum inhibitor assays, summarized in Table V, indicated that K's serum inhibitor content remained within normal limits during his survival time except for a brief interval approximately 19 hours after irradiation, when values increased to twice normal and then rapidly declined to normal levels. These data were in essential agreement with experimental results obtained in rats given 1000 r of total-body x-radiation, where a transitory rise in serum inhibitor titer occurred 48 to 72 hours after exposure.[17]

Table V—Serum Protease Inhibitor

Sample	Hours After Exposure	Inhibitor Units
1	1½	43
2	3½	40
3	5½	50
4	10½	53
5	16	38
6	19	89
7	25	50
8	Post mortem	35
Normal range		37-65

Table VI—Serum Proteins 25 Hours After Exposure

Sample	Total Protein (gm %)	Albumin (gm %)	Globulin (gm %)	γ-Globulin (gm %)	A/G Ratio
Case K	5.2	3.4	1.8	0.4	1.9
Normal range	6-7.5	4.5-5	2-2.5	0.35-1.5	1.2-1.5

Serum Proteins—Electrophoretic examination of two serum samples obtained from Case K at 16 and 25 hours after exposure revealed only two abnormal features. The first was a shift of the alpha globulin peak away from the albumin peak, and the second was a slight diminution in the gamma globulin fraction. The significance of the alpha globulin shift was not readily apparent, but the reduction in gamma globulin has been observed repeatedly in experimental animals and man and appears to be a consistent effect.[2, 18, 19] Case D's serum electrophoretic pattern was not remarkably different from normal with the exception of a slight reduction in the gamma globulin fraction.

Total protein, albumin, globulin, and gamma globulin estimations (Table VI) indicated a general reduction in serum protein content, which was undoubtedly a contributory factor in the severe hypotension which persisted throughout the clinical course of Case K.

Serum Antibodies—The only antibodies demonstrable in K's serum at room temperature were anti-A and anti-B. A variety of techniques were used: routine "back typing" of the serum in test tubes, and checking for atypical antibodies against a panel of eight group O cells designed to demonstrate any one of 23 blood group factors (C, C^w, D, E, V, c, e, K, k, fy^a, fy^b, Js, Le^b, Jk^a, Jk^b, M, N, S, s, P, Lu^a, and Lu^b). The tests were carried out in saline, which was then converted to the indirect Coombs' test. The panel was also ficinized and then converted to the indirect Coombs' reaction after being exposed to K's serum. When group O cells were exposed to K's serum in the presence of group AB serum as a source of human complement in the cold (ice water), they gave a positive indirect Coombs' reaction. This was interpreted as being an example of the "incomplete" cold antibody described by Dacie.[20] There was insuf-

ficient serum to check whether this was a gamma or nongamma antibody.

Alterations in Urinary Constituents Following Acute Gamma-Neutron Exposure

As indicated in the discussion of renal effects in the preceding section, K was anuric for the first 14 hours after exposure (Table III). During the next nine hours, three urine samples were obtained, representing a total volume of 590 ml. The character of these specimens varied markedly: The first was dark, cloudy, and highly concentrated; the second and third were clear and had specific gravities approaching 1. Thus, although a pooled specimen represented a total collection time of 23 hours, direct comparison of analytical results with usual 24-hour collection values did not appear to be justified and values were, therefore, included which permitted comparison on the basis of concentration of the various constituents per unit volume.

Catechol Amine Excretion—K's failure to respond to massive doses of pressor amine was of particular interest. The total amount administered (*l*-arterenol bitartrate) was equivalent to 48 mg of *l*-norepinephrine over a period of 26 hours. Excretion of catechol amines in the urine of patients K and D was measured by established bioassay procedures.[21] The results of these estimations, which are summarized in Table VII, showed K's norepinephrine excretion to be four to five times greater than that determined for normal individuals. This increase undoubtedly reflected administration of *l*-norepinephrine in the infusion, but it is remarkably small in view of the massive dose. Since the pharmacologic response was limited despite the large dose, several mechanisms were considered. Either accelerated destruction in situ, diminished response of effector cells, or local extravasation due to venous incompetence, rather than excretion, must account for the apparent disappearance of active pressor amine. Pressor amine values on D's pooled specimen did not deviate appreciably from normal.

Urinary Amino Acids—Further evidence for a disturbance in nitrogen metabolism was indicated by marked increases in urinary alpha-amino nitrogen excretion in the initial specimens of both Case K and Case D (Table VIII). Quantitative estimations of amino acids appearing in the urine are as yet incomplete, but a preliminary report[22] indicates that they are in essential agreement with qualitative identification by one- and two-dimensional paper chromatography (Table IX). In agreement with a previous report,[6] serine was present only in trace amounts in the heavily irradiated patient,

Table VII—Urinary Excretion of Catechol Amines

Sample	Hours After Exposure	Epinephrine (μg/24 hr)	*l*-Norepinephrine (μg/24 hr)
K pooled	0-22	16.9	233.9
D pooled	0-15	5.8	66.7
Normal range		10-20	25-50

Table VIII—Urinary Amino Nitrogen

Sample	Hours After Exposure	Amino Nitrogen (mg %)
K_1	14	1.120
K_2	17	0.915
K_3	22	0.720
K pooled	0-22	0.860
D_1	4	0.577
D_2	15	0.800
D_3	72	0.766
$Control_1$	....	0.400
$Control_2$	....	0.426
Normal range		0.1-0.4

Table IX—Qualitative Identification of Urinary Amino Acids

Amino Acid*	Case K	Case D
Taurine	Prominent	Prominent
Aspartic acid	+	+
Serine	Trace	+
Glycine	+	+
Glutamic acid	+	−
Threonine	−	+
Alanine	+	+
α-Aminoisobutyric acid	Prominent	Trace
Methionine	+	+
Phenylalanine	+	+
Isoleucine	+	−
Leucine	+	+
Norleucine	+	+

* Solvents: *n*-butanol-formic acid-water (75:15:10), *n*-butanol-propionic acid-water (61:31:8), phenol-water (saturated at 20°C).

K, while excessive amounts of taurine were contained in the specimens of both patients. These data thus offer further confirmation of observations originally made by Kay and Entenman[23] in experimental animals, which indicated a marked increase in taurine excretion following relatively small doses of radiation. The prominence of taurine in the early urine samples of Case D, the less heavily irradiated patient, was the only significant biochemical change observed. Beta-aminoisobutyric acid was readily detected in the urine of K but was barely detectable in the urine of D.

Urinary DNA Metabolites—The appearance of beta-aminoisobutyric acid in the urine of irradiated patients has been interpreted as a reflection of accelerated destruction of deoxyribonucleic acid (DNA) in radiosensitive cells.[24, 25] Increases in total cysteine-sulfuric

Table X—Urinary Cysteine-H_2SO_4 Positive Material

Sample	Hours After Exposure	Mg %
K_1	14	110.0
K_2	17	39.0
K_3	22	28.0
D_1	4	47.5
D_2	15	30.0
D_3	72	43.0
D_4	96	41.0
D_5	120	45.0
$Control_1$	....	44.5
$Control_2$	....	43.0
$Control_3$	....	25.0
$Control_4$	....	42.0
$Control_5$	....	42.0

acid-reacting material[26] have been reported in animals following irradiation,[27] which presumably also reflect a radiation-induced defect in DNA metabolism. Results of measurements of total Dische-positive substances in urine specimens of K and D, as well as a number of normal subjects, are shown in Table X. The first urine specimen voided by K contained approximately twice the amount of cysteine-sulfuric acid-positive material found in normal individuals, while all subsequent samples, as well as voidings from patient D, fell within normal limits. Paper chromatography of a pyridine ethanol (v/v) eluate of urine adsorbed on activated charcoal indicated that the major component of the Dische-positive material in K's urine was deoxycytidine. This conclusion was further substantiated by rechromatography of the ultraviolet-absorbing material corresponding in R_f to deoxycytidine, together with authentic tritiated deoxycytidine of high specific activity.[28] A single spot of ultraviolet-absorbing material containing the radioactive marker confirmed the identity of the compound.

Urinary Creatine and Creatinine—Contrary to recent reports of creatinuria in irradiated experimental animals,[29] no appreciable amounts of creatine were found in the urine of Case K. The analyses in Table XI, performed by the method of Taussky,[30] indicated a greater amount of creatinine in K's first voiding than in subsequent specimens, but the amount contained in the pooled specimen, which approximated a 24-hour collection, was within normal limits. The fact that serum creatinine did not increase appreciably indicated that the aberration in creatine metabolism noted in irradiated animals did not occur during the brief survival time of Case K. A small amount of creatine was found in the 72-hour voiding from D, but urinary creatinine content was normal.

Table XII—Urinary Leucine Aminopeptidase Activity

Sample	Hours After Exposure	β-Naphthylamine (μg/ml/2 hr)	β-Naphthylamine (mg/24-hr sample)
K_1	14	0.52	.....
K_2	17	0.01	.....
K_3	22	0.004	.....
K pooled	0-22	.....	21
Normal range		.....	50-175

Leucine Aminopeptidase—Leucine aminopeptidase is an exopeptidase secreted by the intestinal mucosa, which occurs normally in serum and urine and increases markedly in the urine of patients with metastatic carcinoma involving the bowel.[31] Since the dose of ionizing radiation sustained by K was sufficiently high to anticipate considerable intestinal damage, urinary leucine aminopeptidase activity was determined to ascertain whether such injury would also produce alterations in amount of enzyme excreted. Calculations, based on data shown in Table XII for a pooled sample for the 22-hour period during which voidings were obtained, indicated a normal amount of enzyme activity. However, it was found that virtually all the leucine aminopeptidase activity was in the initial specimen, voided 14 hours after exposure. Since the mode of excretion of the enzyme is not known and the identity of the urinary and intracellular enzymes has not been definitely established, these data are reported only as isolated observations. No attempt was made to interpret their significance in the acute radiation syndrome.

Table XI—Creatine and Creatinine

Sample		Hours After Exposure	Creatine (mg %/sample)	Creatinine (mg %/sample)	Creatine (gm/24 hr)	Creatinine (gm /24 hr)
Urine	K_1	14	0.0	436	.....	.....
	K_2	17	4.0	237	.....	.....
	K_3	22	0.0	217	0.01	1.66
Urine	D_1	4	0.0	208	.....	.....
	D_2	15	6.0	254	.....	.....
	D_3	72	20.0	206	0.249	1.56
Normal range			.....	.....	0.000	1.0-2.0
Serum	K_4	10½	.....	2.0	.....	.....
	K_5	16	.....	2.0	.....	.....
	K_6	19	.....	2.1	.....	.....
Normal range			.....	1.0-2.0	.....	.....

Acknowledgments

The technical assistance of Lora Belle Hughes, Glessie Trafton, and Marguerite Magee is gratefully acknowledged. We should also like to thank Dr. McC. Goodall, Memorial Research Center, University of Tennessee, Knoxville, for performing the bioassay of urinary catechol amines and Dr. Joseph H. Akeroyd, of the Walter Reed Army Institute of Research, Washington, D.C., for carrying out and interpreting the antibody studies.

SECTION IV

Gross and Microscopic Pathology and Neuropathology

C. C. Lushbaugh, M.D.
With the collaboration of Webb Haymaker, M.D.,
of the Armed Forces Institute of Pathology, Washington, D.C.

THREE hours after the death of patient K, a complete necropsy examination was made.

Gross Pathology

External Appearance

The body was that of a middle-aged, male adult weighing 172 lb. and measuring 71 in. in length. The only external evidences of injury were numerous needle puncture marks in both anticubical fossae and in the large veins of the forearms and lower legs, and two recently sutured, 2-cm long, surgical incisions over the manubrium sterni. Both forearms bore blue tatooed designs. There was no erythema of the anterior abdominal wall, and the conjunctivae were no longer hyperemic as they were at the time of admission to the hospital.

Internal Organs

Abdominal Cavity—The subcutaneous tissues and muscles were quite wet, and there was about 250 cc of clear, thin fluid in the abdominal cavity. The peritoneal surfaces were smooth and glistening except those of the first loop of the jejunum, the gastric pyloric bulb, and the surfaces of the left lobe of the liver. These areas were dusky-rose in color and contained minute, petechial hemorrhages. Such hemorrhages were also present in the epigastrium and in the parietal peritoneum. The domes of the diaphragms were at the fourth rib on each side. There was no excessive gaseous distention of the bowel. The majority of the intestines were small in diameter except for the hyperemic first portion of the jejunum. The stomach was moderately dilated, containing about 800 cc of gray, mucinous, gastric contents devoid of food or other recognizable debris.

Pleural Cavity—The lungs collapsed as the chest was opened. The pleural spaces contained less than 10 cc of fluid. The anterior portions of both lungs were well aerated, while the posterior areas were atelectatic. There were no pleural adhesions.

Pericardial Cavity—The pericardial cavity contained about 75 cc of cloudy yellow fluid which contained fibrin that clotted on standing. The right side of the heart was dilated and filled with blood. The left heart was in systole. The pericardium and epicardial fat over the right ventricle which lay in the midline, just above the xiphoid process, contained numerous petechial and small ecchymotic hemorrhages. These hemorrhages were also present in the right auricle and that portion of the right atrium which was most anterior. The distended right auricle appeared to contain thrombosed blood.

Mouth and Pharynx—The oral mucous membranes were normal in appearance and showed no hemorrhages.

Plate I—Photomicrographs of histologic sections obtained at necropsy

A. Femoral bone marrow island (hematoxylin-eosin, ×1,250) consisting of macrophages containing yellow hemosiderin, metamyelocytes, myelocytes, normoblasts, and erythroblasts. No necrotic cells or debris are present. The most primitive and most mature cells are no longer demonstrable.

B. Femoral bone marrow (Prussian-blue reaction, ×330) showing reticular macrophages loaded with bright blue irregular masses of iron among the pink-staining myelogenous cells and orange-staining erythrocytes.

C. Peripheral pulmonary alveoli (Prussian-blue reaction, ×200) containing masses of clumped macrophages filled with ingested material and erythrocytes which stain positively for iron.

D. Chromatin debris in a cortical follicle of a mediastinal lymph node (hematoxylin-eosin-azure, ×320).

E. Thymus gland (hematoxylin-phloxine, ×260) showing small focus of remaining lymphocytic debris, and epithelial-like groups of reticular endothelial stromal cells.

F. Typical remnant of a lymphoid follicle in the spleen (hematoxylin-eosin-azure, ×330) showing the apparent hypertrophy of the central reticular macrophages.

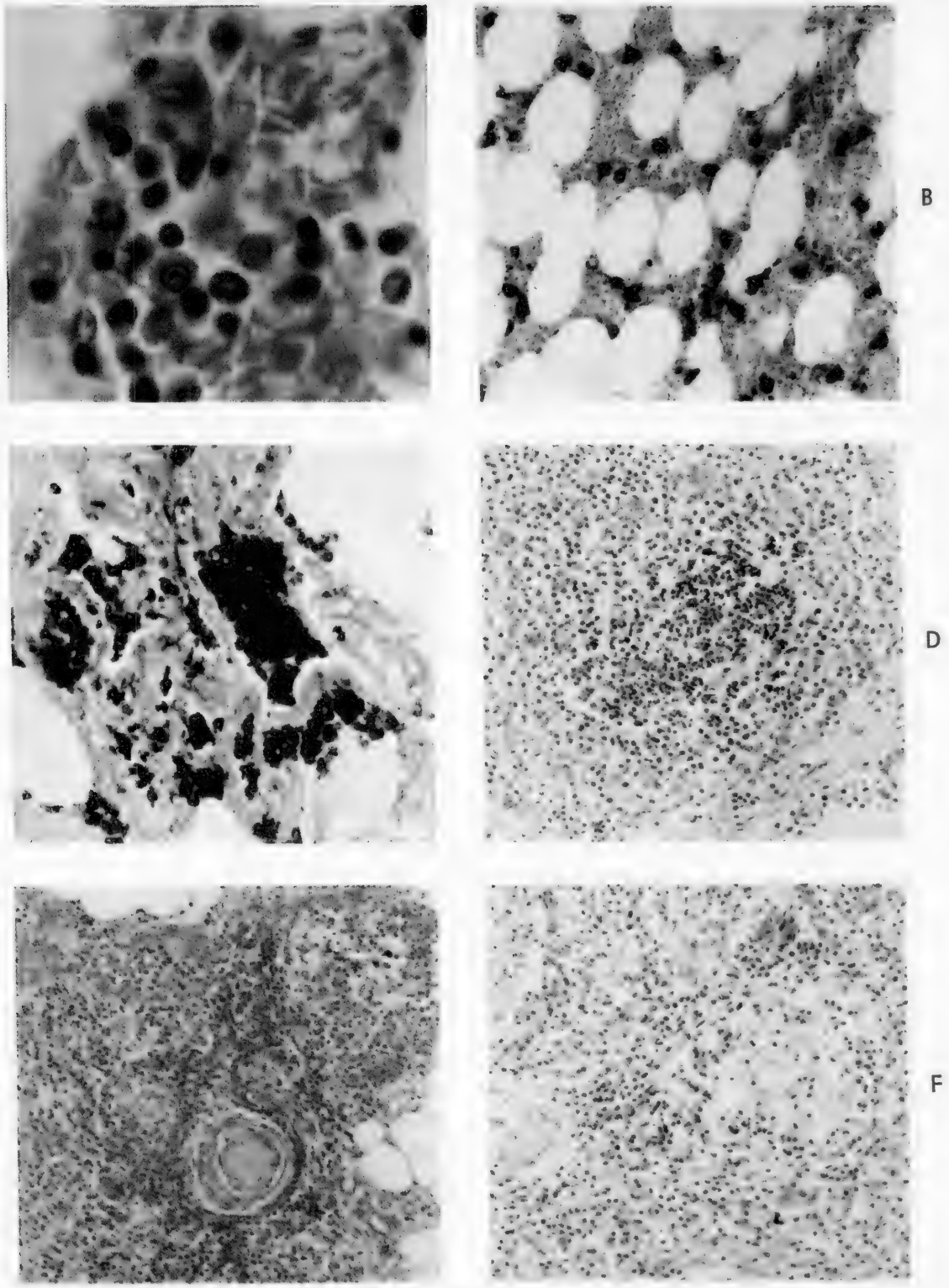


Plate I—See description at left.

Thyroid and Thymus—The thyroid was normal in size, shape, and consistency. There were some small lymph nodes associated with it which appeared grossly to be normal. The site of the thymus was filled with fat in which there could be seen some minute remnants of thymic gland. There were no hemorrhages in the thymic fat or other mediastinal structures.

Trachea and Main Bronchi—The mucosa of the trachea and main bronchi appeared edematous, but these tubes did not contain frothy edema fluid and no such fluid could be expressed from the lungs. The tracheobronchial lymph nodes were anthracotic. One in the left hilus contained a 5-mm-diameter, round, calcified nodule. There was a similar calcified nodule under the pleura of the left upper lobe in the intralobular fissure. Besides their black color, these hilar nodes were conspicuous only because of their soft, fleshy consistency.

Lungs—The right lung weighed 400 gm; the left lung, 450 gm. Their posterior portions were atelectatic, while their anterior portions were well aerated. There were no areas of consolidation or hemorrhage. The left lung contained the Ghon complex described above. The lung parenchyma contained irregular anthracotic blotches (up to 2 cm in size) uniformly distributed throughout.

Heart—The emptied heart weighed 400 gm. The tricuspid, pulmonary, and aortic valves were normal. The mitral valve showed slightly more than moderate thickening of the free margins, and some shortening and thickening of the chordae tendinae were seen. The right ventricle averaged 4 mm in thickness; the left, 18 mm. The right ventricle and atrium were dilated. The auricle of the right atrium contained thrombosed blood between the pectinate muscles, and there were many pericardial and intramuscular linear petechial hemorrhages in the right atrium and right ventricle. The left ventricle did not have these hemorrhages except in the interventricular septum, where they were most prominent just below the aortic valves. The coronary blood vessels showed minimal atherosclerosis and no thrombosis. The aorta contained only a moderate amount of atherosclerosis in its lower third. The great veins were normal.

Liver—The liver weighed 1,950 gm. It was acutely congested, as evidenced by its dark color and by extremely prominent central areas which gave its cut surfaces a typical nutmeg pattern. The peritoneum over the left lobe of the liver was slightly opaque, and there were small areas of hemorrhage under it. On section, these areas appeared to be continuous with the vascular spaces of the liver.

The gallbladder was distended with about 50% more bile than is normal. The bile, however, was easily expressed through the papilla of Vater and was green, thin, and mucinous. There were no gall stones.

Pancreas—The pancreas appeared normal throughout its length.

Spleen—The spleen weighed 116 gm. Its capsule was wrinkled, and the organ was exceptionally flabby. On the cut surfaces, the connective tissue trabeculae were unusually prominent and the pulp, while bloody, appeared to be much more fluid than usual. No lymphoid aggregates could be discerned.

Gastrointestinal Tract—The stomach was distended with slightly less than 1 liter of thin, mucinous, gray fluid with a typical gastric odor. The peritoneum over the antrium was dusky-rose and contained many hemorrhages, while under this area the mucosa anteriorly and posteriorly also contained numerous petechial hemorrhages. These hemorrhages were seen only within a radius of 5 cm from the pylorus. The mucosa of the duodenum and jejunum appeared pale and edematous except in the region of the first 10 cm of the jejunum, which was moderately dilated and had a hyperemic mucosa. There were, however, no grossly discernible ulcerations in this or any other portion of the intestinal tract. The jejunum became progressively smaller in diameter caudally, so that the ileum and colon were quite contracted and free of fecal material and intestinal chyme other than mucus. The appendix appeared to be atrophic. The mesenteric lymph nodes were small and difficult to discern from the surrounding fat, since both were pinkish-yellow.

Adrenal Glands—Both adrenals were normal in size and shape. They weighed (with a small amount of fat) 7 gm each. Surfaces made by cutting failed to reveal any abnormality. The cortices appeared normally lipid-rich.

Kidneys—The right kidney weighed 130 gm; the left, 140 gm; and the capsules stripped with ease. The parenchymal blood vessels were hyperemic. The surfaces made by cutting bulged slightly so that the edges could not be completely approximated. The markings of the cut surfaces were those of grossly normal kidneys.

Gastrourinary Tract—The renal pelves, ureters, and urinary bladder were normal in appearance. The urinary bladder was contracted and contained only about 3 cc of yellow, cloudy urine. The lining of the bladder was thrown up into folds and contained no hemorrhages.

Generative Organs—The prostate was normal in size, although there was a hypertrophic

median bar. This median bar was knobby and had a mulberry-like appearance.

The testes were normal in size but small. The testicular tubules could be teased apart easily.

Skeletal and Muscular System—There were no gross abnormalities of the bone other than the recent surgical biopsy of the manubrium sterni. The bone marrow appeared hemorrhagic and devoid of its normal, fleshy appearance.

The muscles were dark red and much more moist than normal. Rigor mortis was exceptionally strong and the muscles more contracted than usual. The muscles and subcutaneous tissues of the arms and thorax showed extensive rigor mortis and swelling, but this was not evident in the lower portion of the torso and the lower extremities (five hours post mortem).

Cranial Cavity—The brain stretched the dura mater tightly and was congested and swollen. It weighed (including the dura) 1,600 gm. The gyri were flattened and the sulci obscured. The blood vessels were prominent. There was a small pressure conus in the region of the uncus hippocampi. A section of the brain revealed congestion of the white matter of the cerebrum and, in the parietal lobe, several prominent red-tinged streaks along the course of the vessels.

The pituitary gland was quite hyperemic, fleshy, and soft in appearance.

Microscopic Pathology

Fixation of the hematopoietic tissues was obtained with Maximow's Zenker-formol solution, of the brain and other neurological tissues with neutralized formalin, and of the other organs with mercuric chloride formalin solution. In addition to hematoxylin and eosin, Maximow's hematoxylin-eosin-azure stain, a Prussian-blue stain for iron, the periodic acid Schiff reaction, and Verhoeff's elastic tissue stain were used in the histologic preparations.

Bone Marrow—Sections were obtained from marrow in the proximal femur, vertebral bodies, and sternum. The marrow specimens from these areas were histologically quite similar, but the staining of the femoral marrow was best since no decalcification was necessary. A search for mitoses failed to reveal a single one in any of the sections. Similarly, there were no cells of either the myelocytic or the erythropoietic series which showed any destruction in situ (Plate I *A*). Bone marrow islands contained more red cells than nucleated cells, and there was a pronounced decrease in polymorphonuclear leukocytes and primitive cells in particular. Eosinophilic myelocytes were prominent along with the very primitive reticuloendothelial macrophages which contained frequent irregular-sized blobs of gold pigment and many pyknotic cell remnants. The Prussian-blue stain for iron made these cells stand out prominently, since the gold pigment and the diffuse brown cytoplasm of these cells now stained positively blue (Plate I *B*). Occasional megakaryocytes were found to have degenerate, pyknotic nuclei, but nuclear debris were never found freely in any of the sections. When present, such debris was always inside the reticular histiocytes. The vertebral marrow showed slightly severer depletion than the femoral marrow, as many of the spaces formerly filled by cells were found here to contain protein-rich edema fluid. The majority of the nucleated cells here were erythro- and normoblasts. As in the femoral marrow, no mitotic activity was present, and the primitive hemocytoplasts in all series were conspicuously difficult to find.

Lungs—There were occasional areas of alveoli containing thin, protein-containing fluid. The lungs were poorly expanded, and there were many areas of focal atelectasis interspersed with areas where the alveoli were ballooned by emphysema with the walls being ruptured. Many areas were found where there were relatively huge atrial cavities. In the alveoli near the periphery of the lungs and in the atelectatic alveoli adjacent to the bronchi and interlobular septa there were many macrophages collected in masses containing yellowish-green granular debris, some of which still had the form and appearance of erythrocytes. These macrophages stained positively for diffuse and particulate iron (Plate I *C*). They were occasionally found associated with macrophages containing carbon pigment in the interstitial tissue. In addition, the alveolar septa contained an abnormal number of polymorphonuclear leukocytes. There was so much iron present in the macrophages that it was difficult to believe this picture resulted from the radiation. No gross hemorrhages were found. The fact that this man had had pneumonitis in the past was evidenced by epithelization of many of the peripheral alveoli, and many of the macrophages were associated with this epithelium. On the other hand, it was in these areas that one saw degenerating granulocytes, lymphocytes, and extravasated red cells being ingested by the macrophages. Many of the iron-laden macrophages were in the bronchioles and bronchi, apparently in the process of being coughed up. Sections containing pleura showed damaged (pyknotic and crenated) serosal nuclei and many pyknotic and degenerating lymphocytes and granulocytes in the subpleural connective tissue.

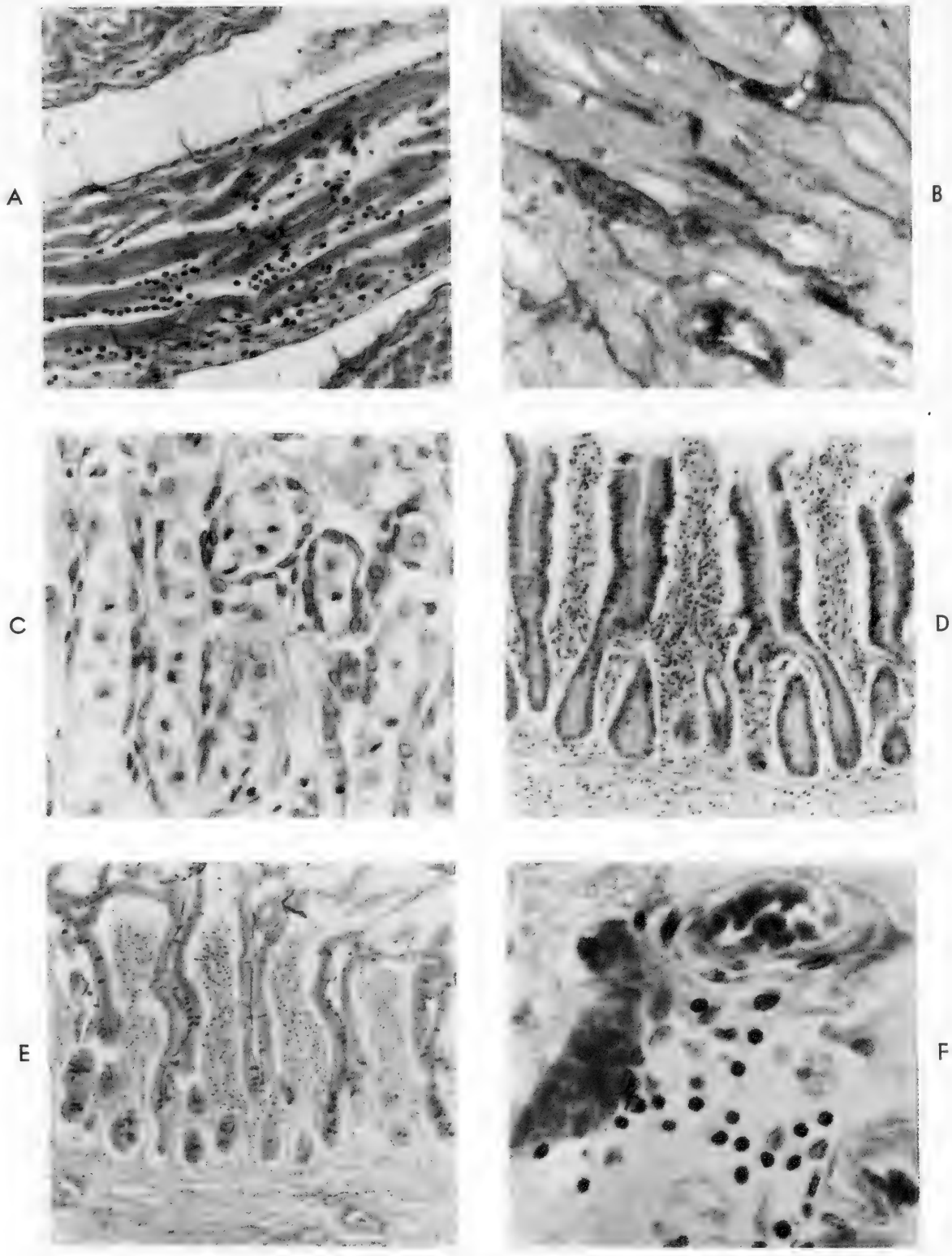


Plate II—See description at right.

Tracheobronchial Lymph Nodes—Mucus in the bronchi contained desquamated columnar epithelial cells, macrophages laden with iron, and a few exudated granulocytes. Whether blood was present ante mortem could not be determined. The peribronchial lymph nodes contained carbon dust in macrophages in areas of increased collagenous connective tissue. The iron stain revealed foci of iron-containing macrophages. These foci were usually in or around areas of anthracosis. The cortical sinuses contained macrophages, but very little stainable iron, although some dark blue blobs were present. In another lymph node from the hilus, iron-laden macrophages were found most prominently in the peripheral sinus and the perifollicular sinuses.

Lymph Nodes (in general)—The lymph nodes in general were markedly atrophic owing to the recent loss of lymphocytes. The architecture was quite recognizable, and the reticulum and the sinusoidal macrophages were particularly prominent. There was a variable amount of lymphocytic debris present; a periaortic node from the celiac axis showed the least amount of lymphocytic debris but the greatest amount of atrophy. The reticular centers of follicles were not prominent, and there was no apparent increase in sinusoidal phagocytosis, although some leukocytes were present. Many of the remaining lymphocytes were small and pyknotic, although many normal-appearing lymphocytes were present. Relatively more debris was found in the lower abdominal lymph nodes, together with an occasional reticular center. Occasional nodes from this region contained large numbers of leukocytes in the sinuses. Lymph nodes from higher up in the mediastinum and lower down in the abdomen showed follicles rich in chromatin dust (Plate I *D*).

Thymus—The thymus consisted of thin strands of reticular cells with occasional large Hassall's bodies. Either there were very few lymphocytes before the accident or, as is more likely the case, since macrophages containing vestiges of cellular debris could be seen, the lymphocytes present at the time of the accident were destroyed and removed. The lymphocytes still present at the time of death were extremely pyknotic, and many peculiar "explosion figures" were seen which typified continuing rhexis. Some of the reticular cells were hypertrophied and arranged in epithelial-like clumps (Plate I *E*).

Spleen—The lymphoid follicles were greatly depleted. They were now composed of large reticular cells, a few scattered lymphocytes, the majority of which were normal in appearance, and numerous large macrophages containing vacuoles (Plate I *F*). The red pulp was composed of islands of erythrocytes, among which were many pyknotic white cells. The sinusoids, however, were far from being completely distended, and there were many areas in the pulp where there were no red cells other than a few apparently dead ones mixed among degenerating leukocytes. The reticuloendothelial cells in these areas were large and often filled with red and white cell debris. The stain showed such macrophages staining positively for iron, but not to the same extent as in the bone marrow and lungs. In addition, in the relatively bloodless areas of the pulp there were diffuse, fine reticular-like fibers which stained positively for iron.

Appendix—The appendiceal mucosa was hyperchromatic, and the lamina propria was lymphoid-poor. The submucosal follicles contained large reticular centers in which a few of the reticular histiocytes still contained chromatin dust. These centers were surrounded by pyknotic, crenated lymphocytic nuclei. The mucus of the lumen was free from fecal debris but contained masses of degenerating leukocytes. An occasional vein of the mesoappendix contained fibrinous leukocytic clots.

Heart—The serosal cells of the pericardial surface were swollen and bead-like with minute strands of fibrin adhering to them. The connective tissue bands between the fat cells were widened by abundant protein-rich edema fluid. There was fibrinoid necrosis of the small collagenous fibers immediately beneath the serosa, where granulocytes had accumulated in minute foci, often around small arterioles. These ac-

Plate II—Photomicrographs of histologic sections obtained at necropsy (continued)

A. Interstitial accumulation of granulocytes between myocardial muscle fibers in the base of the right ventricular wall (Verhoeff's elastic connective tissue stain, ×330).

B. Swollen Purkinje myocardial fibers from the right atrial appendage showing perinuclear vacuolation and interfibrillar edema (Verhoeff's stain, ×500).

C. Gastric mucosa (PAS stain, ×650) from anterior wall of stomach showing intraglandular sloughing of pyknotic parietal cells.

D. Duodenal-jejunal mucosa (hematoxylin-eosin, ×210) showing loss of epithelium of villous tip, decreased cellularity of the lamina propria, absence of mitoses, and absence of signs of epithelial necrosis.

E. Lower jejunal mucosa (PAS stain, ×125) showing edema of villa and disruption and beginning intraluminal loss of the epithelium.

F. Leptomeninges of the cortex (hematoxylin-phloxine, ×450; AFIP 905226-15) showing perivascular exudation of lymphoid cells and leukocytes, and activated histiocytes containing blood pigment.

cumulations of leukocytes were also found in the pericardium immediately adjacent to the myocardium and in the interstitial connective tissue of the right myocardium itself, along with diffuse irregular hemorrhages (Plate II *A*). These exudates were oriented in a hit-or-miss fashion and were most frequent in sections from the base of the right myocardium, but infrequent in sections from the apex and left ventricle. Interstitial hemorrhages were common among the muscle fibers of the right auricular appendage and atrium.

The myocardial fibers did not show loss of striations or any other degenerative signs, but the Purkinje fibers of the right atrium were unusually swollen in appearance (Plate II *B*). The nuclei of these fibers were swollen and irregularly enlarged, misshapen, and surrounded by large clear spaces, which were interpreted as perinuclear accumulations of edema fluid. Sections obtained from the same areas of the heart of a man of similar age, muscular activity, and history of accidental sudden death failed to show this remarkable swelling at all. Interstitial edema was present throughout the entire myocardium and seemed to explain the unexpectedly heavy weight of the emptied heart (400 gm). The blood of the myocardial vessels was low in leukocytes, but the thrombi between the pectinate muscles of the right auricle and atrium were composed principally of granulocytes and fibrin.

Liver—The histologic appearance of the liver was quite different from what was anticipated from its gross appearance. The central areas did not show much atrophy, and the engorgement seen grossly was apparently lost during fixation. The iron stain showed relatively little iron deposition. There was a yellow-brown pigment in the central hepatic cells which failed to stain positively for iron. The hepatic cells contained fine granules of iron, but the most strongly positive areas were found in occasional macrophages located in the midcentral zones. No macrophages were found which stained as positively for iron as those of the bone marrow and lungs. Aside from the early central atrophy, there was no evidence of primary or secondary hepatic cell injury.

Kidneys—The convoluted tubules showed a slight amount of cytoplasmic sloughing, while in the medulla, occasional tubules were filled with eosinophilic, cytoplasmic debris.

Gastrointestinal Tract—Esophagus: The esophageal epithelium was covered with a thin layer of poorly stained erythrocytes. There was a well-defined basal, glomerular, and squamous layer. A search along the basal layer showed that no mitoses were present. There was an occasional vacuole containing a lymphoid-like cell in the epithelium, while the basal cells appeared to be differentiating into squamous cells. The nuclei were swollen and more vesicular than normal, and even the most basal of these cells appeared to have developed intercellular bridges which were accentuated by intercellular edema. In the subepithelial connective tissue, there was an increase in the numbers of lymphoid and polymorphonuclear cells. An occasional lymphoid follicle was present containing chromatin dust which was both free and in macrophages. There was a reduced number of normal-appearing large and medium-sized lymphocytes in these follicles. There was no true arteritis or phlebitis. The smooth muscle coats were edematous. The blood in some of the smaller vessels of the periesophageal mediastinal connective tissue stained opaquely as though it were congealed. In these vessels there was seen an occasional leukocyte undergoing rhexis.

Stomach: The gastric mucosa was, in general, well preserved. The most superficial portions showed foci of autolytic changes. In the best-preserved areas, many acid-secreting eosinophilic chief cells could be found free in the lumen of the glands. These sloughed cells usually had crenated, pyknotic nuclei, although the nuclei were occasionally swollen and vesicular (Plate II *C*). These changes were seen in the stomachs of the heavily irradiated monkeys as one of the earliest signs of heavy radiation exposure.[32] The zymogen cells appeared to be unaffected. The subperitoneal connective tissue was extremely edematous. In this edematous fluid, there were occasional leukocyte-like cells rimmed by dark blue to purple, opaque material, irregular in outline which gave them a "fried egg" appearance. There was an increase in leukocytes in the connective tissue here, and occasional veins were occluded by fibrin and leukocyte masses. The blood vessels themselves did not appear to be chemotactic. Sections from the posterior gastric wall did not show a similar necrosis of the parietal cells.

Duodenum: The most superficial layers of the duodenal mucosa were missing. Fragments of epithelial strips were lying free in the lumen, and occasionally a well-preserved villus with epithelium could be found. Such villi showed a loss of small lymphocytes from the connective tissue core. There was shrinkage of the core with condensation of the reticular cells and histiocytes (Plate II *D*). Scattered among these cells were occasional pyknotic remnants of lymphocytes and granulocytes. Such remnants could also be seen in the overlying epithelium, which

contained occasional mucous vacuoles. These mucous vacuoles were found also in the deepest cells of the crypts. No mitoses were present here. Outside of the pyknotic nuclear remnants, the only other change in the crypts consisted of nuclear ballooning. Necrosis of the crypt epithelium was not found. Brunner's glands showed cells which were occasionally without a nucleus or with a distorted and pyknotic one. Most, however, appeared unaffected.

Jejunum: The section of jejunum was taken from the area of subperitoneal hemorrhage and edema. The extravasated red cells could be seen diffusely through the subperitoneal edematous connective tissue, and there had been a slight leukocyte exudation. In addition, in and around some of the smaller blood vessels leukocytic, nuclear debris could be found along with leukocytic nuclei elongated in the process of diapedesis. Some of these vessels were occluded by opaque masses of erythrocytes in which it was difficult to delineate individual red cells. The Meissner-Auerbach plexus and the sympathetic nerves were quite edematous. The jejunal mucosa was better preserved than in the duodenum. Villi could be seen which were still covered completely by epithelium (Plate II *E*). No mitoses were present in the crypts. The nuclei showed ballooning. A few examples of intraepithelial nuclear debris could be found, but the crypts filled with debris as found in heavily irradiated animals were not found here. Pyknotic leukocytes and lymphocytic remnants were present in the lamina propria, which was relatively cell-poor and shrunken. The epithelial cells of the extrusion zone of the tip of the villus were lower and broader than those along the side of the villus. True early squamous metaplasia was seen best in the necks of the crypts.

Lower Jejunum: Similar changes were seen.

Ileum: The omental fat showed no changes. The lymphoid tissue of the villi was markedly depleted. The villi were, in general, shortened and there was an apparent increase in mucous goblet cells. No mitoses were found. An occasional crypt contained cellular debris.

Pancreas—The pancreas showed normal-appearing islets and acini. An occasional necrotic cell in the pancreas proved, on close examination, to be leukocytic in origin.

Prostate—Some of the prostatic glands were hyperplastic and showed a squamoid metaplastic type of epithelium which, in some areas, was definitely transitional.

Pituitary—The pituitary blood vessels were quite hyperemic, and in the region of the stalk there were areas of extravasated red blood cells.

Brain and Spinal Cord—In general, the changes in the meninges were few. There was conspicuous engorgement of vessels in the meninges, brain substance, and choroid plexuses. In several sections substantial activation of arachnoidal histiocytes was observed. Here and there, some of the histiocytes had become macrophages and, on rare occasion, macrophages were found filled with broken-down blood pigment (Plate II *F*). A few neutrophilic leukocytes were found in the arachnoidal meshes. In the meninges no vasculitis was observed except for a few small and large mononuclear cells in the adventitia. Most of these were regarded as activated histiocytes rather than lymphocytes. No collagen damage was observed except possibly in occasional short stretches of the arachnoidal membrane, beneath which the arachnoidal trabeculae were condensed or swollen and displayed increased eosinophilia.

Conspicuous in the brain substance was focal evidence of an edematous process perivascularly, especially in the cerebral white matter, and occasionally in the gray matter. This was manifested by porosity of perivascular brain tissue. No coagulated edema fluid was found in the brain, apparently since only low-molecular fluid had escaped from the blood stream. The prominent red-tinged streaks noted grossly in the cerebral white matter proved microscopically to be due to the presence of low-molecular fluid and erythrocytes in the perivascular white matter. Tissue sponginess, denoting an edematous process, was noted here and there in lamina I of the cerebral cortex, and sometimes in lamina II.

In the brain substance no vasculitis was observed, but the adventitia of vessels, chiefly veins, contained mononuclear cells. Such cells were usually few in number. Vessels thus affected were found chiefly in the cerebral white matter where some of them contained plugs of leukocytes or plugs of leukocytes in clotted plasma. A fair number of leukocytes in several vessels exhibited karyorrhexis and other cytologic evidence of damage.

Occasionally in the cerebral cortex a necrotic nerve cell was found. In the white matter of the parietal lobes an extraordinary number of oligodendroglia were pyknotic. The cytoplasm of numerous astrocytes (or oligodendroglia) in the corpus callosum was rather copious, which was considered of a reactive nature. No alterations were observed in the white matter proper.

The choroid plexuses of all ventricles were studied. The only abnormality found consisted of one small group of mononuclear cells in the base of the choroid plexus of the fourth ven-

tricle. Here, occasional macrophages contained broken-down blood pigment. The ependyma was spared except for local loosening of the subependymal matrix in the floor of the fourth ventricle (in the region of the dorsal nucleus of the vagus nerve bilaterally), and except for a rather large, old glial scar in the wall of the lateral ventricle.

The cerebellar cortex was unaffected except for the tonsil; it was edematous, and a fair number of the granule cells were poorly stained. No pyknosis of granule cells was observed. This edematous process was thought to be related to circulatory disturbances consequent to pressure of the tonsil against the lower brain stem, secondary to brain swelling. Some of the cells of the dentate nucleus appeared unduly shrunken.

Hemorrhages were fairly common throughout the brain but were small and usually confined to the perivascular space. They were most common in the hypothalamus and in the medulla oblongata, especially near the ventricular system. Because of lack of cellular reaction perivascularly, they were regarded as an agonal phenomenon.

In summary, the microscopic evidence indicated circulatory disturbance in the brain, manifested by generalized cerebral swelling perivascular transudates and hemorrhages. There was no appreciable vasculitis, but reaction on the part of the histiocytes was very evident in the arachnoidal meshes and, in less measure, about vessels in the meninges and brain. Lymphocytes also contributed to the infiltrates, including the one found in the choroid plexus. The brain swelling and edema could be explained by the right cardiac failure and resulting cerebral passive congestion and anoxia.

Anatomical Diagnoses

The anatomical diagnoses which summarized the gross and histologic findings were as follows:

Acute myocarditis, right atrium and ventricle; severe intracellular myocardial edema.

Acute cardiac dilatation, right atrium and ventricle (clinical right heart failure).

Acute pericardial fibrinous effusion, inflammation and edema.

Thrombosis of the right auricular appendage.

Acute hepatic central congestion.

Cerebral edema; slight cerebellar pressure conus; diffuse radiovasculitis, agonal perivascular cerebral hemorrhages; parietal oligodendroglial pyknosis.

Acute radioatrophy of spleen, lymph nodes, thymus, and bone marrow; lymphorrhexis in lymph nodes and thymus.

Peripheral leukocytosis and lymphopenia.

Acute radiohemachromatosis of macrophages of bone marrow and lungs.

Petechial hemorrhage (and radiovasculitis) of epigastrium, pericardium, left lobe of liver, jejunal and antral peritoneum, antral mucosa, pericardium, right atrial, ventricular, and interventricular septal myocardium.

Acute, moderate gastric distention.

Radionecrosis of gastric parietal cells of anterior gastric wall.

Acute upper jejunal distention.

Acute, generalized mitotic radiosuppression seen in gastrointestinal tract, skin, esophagus, bone marrow, lymph nodes, and testes.

Acute jejunal and ileal radioenteritis.

Moderate distention of gallbladder.

Early benign prostate hyperplasia, median bar type.

Fibrocalcareous complex of Ghon.

Minimal pulmonary anthracosis and anthracosis of peribronchial and hilar nodes.

Acknowledgments

Special acknowledgment and credit is here given to Gretchen Humason and Julia Wellnitz for their highly successful work in the preparation and photography of the tissue sections.

SECTION V

Special Studies

Wright H. Langham, Ph.D.
With the collaboration of Donald F. Petersen, Ph.D.,
R. Gordon Gould, Ph.D., Harry Foreman, M.D., F. N. Hayes, Ph.D.,
Marvin Van Dilla, Ph.D., Morris F. Milligan, Ph.D., William D. Moss, B.S.,
Dean D. Meyer, B.S., and others

A NUMBER of special biochemical studies, whole-body counts, and gamma-ray spectral measurements were performed to collect additional information on effects of high doses of radiation and to provide data for dose calculations and for comparison with similar data obtained from past cases of serious exposure. In the case of K, the number of studies that could be carried out was limited by the condition of the patient, which affected the amount of antemortem biological material available for study. Prior to death, the patient voided only three times, with a total urinary output of only 590 ml. The biological samples available for study were as shown in Table XIII.

No concerted effort was made to carry out special biochemical studies on the other personnel involved in the accident, since the exposures were all relatively low. Some measurements were made, however, on Case D, who received an exposure of about 130 rads (most of which resulted from his entering the room soon after the accident had occurred).

Measurement of Induced Sodium-24 Activity

Blood—The first samples of blood were drawn from K at 6:10 p.m., and from D at 8:30 p.m. They were counted immediately for induced Na^{24} activity and for comparison with similar measurements made on victims of previous Los Alamos criticality accidents.[1] Five milliliters of blood was counted in a sodium iodide crystal well counter which, when calibrated against a Na^{24} standard, had an efficiency of 8.1%. Corrected to zero time, K's blood showed a Na^{24} activity of 5.47 mμc/ml. From his hematocrit of 58% and a serum sodium concentration of 3.33 mg/ml, his serum sodium specific activity was estimated as 3.9 mμc mg. A similar measurement using a 9½ × 6 in. sodium iodide crystal spectrometer gave a Na^{24} blood concentration of 5.13 mμc/ml and a serum sodium specific activity of 3.66 mμc/mg (average 3.77 mμc/mg). The specific activity of D's serum sodium measured by the same

Table XIII—Biological Samples Available for Study (Case K)

Urine	
Voided 6:30 a.m. 12/31/58	150 ml
Voided 10:00 a.m. 12/31/58	180 ml
Voided 2:40 p.m. 12/31/58	260 ml
From bladder at autopsy, 6:30 a.m. 1/1/59	3 ml
Feces	
Formed stool 5:20 p.m. 12/30/58	36 gm
Diarrhea fluids 5:25 p.m. 12/30/58	64 gm
Second diarrhea 7:30 p.m. 12/30/58	Not available
Blood	
6:10 p.m. 12/30/58	30 ml
8:00 p.m. 12/30/58	20 ml
10:00 p.m. 12/30/58	20 ml
3:15 a.m. 12/31/58	20 ml
8:30 a.m. 12/31/58	20 ml
11:15 a.m. 12/31/58	20 ml
12:30 p.m. 12/31/58	20 ml
5:15 p.m. 12/31/58	20 ml
6:30 a.m. 1/1/59	Post mortem
Tissues (for analysis)	
Heart	371 gm
Lungs	854 gm
Stomach	203 gm
Jejunum	169 gm
Ileum	91 gm
Colon	160 gm
Skeletal muscle	199 gm
Liver	619 gm
Kidneys	252 gm
Spleen	108 gm
Thymus	25 gm
Pulmonary lymph nodes	5.2 gm
Adrenal	3.5 gm
Rib	19 gm
Sternal bone	122 gm
Vertebral bone	180 gm
Sternal cartilage	40 gm

Table XIV—Serum Sodium Specific Activities of Los Alamos Criticality Accident Victims (at t = 0)

Case*	Serum Na S. A. (mμc/mg)
1	0.49†
2	0.03
3	1.99†
4	0.36
6	0.19
7	0.10
8	0.05
9	0.04
10	0.03
D	0.01
K	3.77†‡

*Case numbers are those in the paper by Hempelmann et al.[1]

†Terminated fatally.

‡Average of crystal spectrometer and sodium iodide well counter determinations.

methods was = 0.01 mμc/mg, which is approximately the lower limit of detection. The radioactivity in the blood was characterized as Na^{24} both by its 2.76-mev gamma-ray energy and its half-life (= 14.5 hr).

A comparison of the serum sodium specific activities with those of previous criticality accident cases is shown in Table XIV. These data were the first laboratory indications that K had received a supralethal exposure. Assuming the same ratio of serum sodium activation to radiation dose as occurred in Cases 1 and 3, K's serum sodium value indicated an exposure that was approximately eight times the dose that had been fatal in 24 days to Case 1 and approximately two times the dose that had proved fatal in 9 days to Case 3. D's serum sodium value indicated relatively little exposure to the prompt radiation, indicating that the majority of his exposure resulted from his entering the room after the accident had occurred.

G. S. Hurst, of the Oak Ridge National Laboratory, was able to give a preliminary estimate of the dose received by K based on his experiences during and subsequent to the Y-12 accident.[33] His estimate of the fission neutron dose was based on his observations that a burro exposed to 48 rads of fission neutrons in a mock-up experiment showed 2.9×10^{-1} mμc Na^{24}/ml of blood. Assuming that the accidents were comparable and that the blood sodium concentrations in the burro and in man were the same, the neutron dose received by K was estimated as

$$\frac{5.47 \times 48}{0.29} = 900 \text{ rads}$$

Assuming a gamma-to-neutron ratio of 3 (observed in the mock-up of the Y-12 accident), the estimated gamma dose was 2,700 rads, giving a total exposure of 3,600 rads.

Table XV—Total-Body Sodium-24 Measurements (t = 0) on Personnel in Building at Time of Accident

Initial*	Occupation	Sodium-24 Activity (μc)
K	Chemical operator	293†‡
D	Chemical operator	1.1‡
		1.1
R	Chemical operator	0.60
L	Security inspector	0.15
M	Security inspector	0.14
Z	Operator supervisor	0.14
X	Chemical operator	0.05
U	Monitor	0.04
N	Chemical operator	<0.02
O	Chemical operator	<0.02
W	Group leader	<0.02
S	Monitor	<0.02
P	Security inspector	<0.02
Q	Security inspector	<0.02

*Designations of individuals are the same as those used in Section VII

†Post mortem, after correcting for Na^{24} loss in urine and feces prior to death

‡Measured by gamma spectrometer; all other measurements in whole-body liquid scintillator

Similarly, the neutron radiation dose received by D was estimated at 2.6 rads. In his case, use of a gamma-to-neutron dose ratio of 3 to obtain prompt gamma exposure was not justified. Serum sodium specific activities were not measured on any of the other personnel in the building at the time of the accident.

Whole-body Sodium-24 Measurements—All persons in the building at the time of the accident were counted for gross whole-body gamma activity in the whole-body liquid scintillation counter within three hours after the accident. D was also counted in the whole-body gamma-ray spectrometer, as was the body of K. No whole-body measurements were made on K prior to death because of his condition and the fact that his body Na^{24} activity immediately after the accident exceeded the capacity of the counters. The Na^{24} measurements (corrected to $t = 0$) on all personnel are shown in Table XV.

A gamma-ray spectrometer measurement on Case D indicated conclusively that the principal activity measured in the various personnel was Na^{24}. His spectra, taken at 4 and 70 hours after the accident, showed a 15% loss of Na^{24} during the interval, which is in good agreement with the value of 13% predicted from whole-blood Na^{22} studies on humans conducted by Richmond.[34]

The value reported for K was corrected for

loss of 1 μc of Na^{24} in urine, feces, and diarrhea fluid prior to death. Because of the high Na^{24} activity of the body, it was not possible to make the spectral measurements with the 9½ × 6 in. sodium iodide crystal spectrometer, and it was necessary to substitute a 3 × 3 in. crystal and make the measurements at a distance of 46½ in. from the sternum. The counting system and geometry were then calibrated by giving a known amount of Na^{24} to six subjects varying in weight from 125 to 214 lb and counting them in exactly the same position. From the calibration curve of weight versus counts and K's weight, it was possible to estimate his Na^{24} activity rather accurately. Corrected for excretion and for radioactive decay, his body Na^{24} activity at the time of the accident was estimated at 293 μc. The application of blood and body Na^{24} measurements to neutron dose calculations is shown in Section VI.

Sodium-24 Measurements on Autopsy Specimens (Case K)—Since sodium is largely extracellular, soft tissues having about the same amount of extracellular fluid would be expected to contain approximately the same amount of sodium. Exceptions are the lymph nodes and blood, which contain relatively larger amounts of extracellular fluid, and muscle, which contains a large amount of intracellular but a relatively small amount of extracellular fluid. Bone, however, contains more sodium than do the soft tissues; about 50% of this sodium is incorporated in the bone mineral and is unexchangeable. The measured Na^{24} activity in the autopsy specimens from K (corrected to time of the accident) are shown in Table XVI. All samples were measured with the large sodium iodide crystal gamma spectrometer, which was calibrated with a known Na^{24} standard.

Division of the total Na^{24} activity of the soft tissues by the gross soft tissue weight gives a Na^{24} activity of 2.93 mμc/gm. If the sodium space is taken as $\frac{Na^{24}/gm\ tissue}{Na^{24}/gm\ serum}$, K's sodium space is estimated as 24.7%, which agrees with the value of 25% reported by Hevesy.[35] Assuming the specific activity of the total-body sodium was the same as that of serum sodium (3.77 mμc/mg), K's total-body sodium content would be

$$\frac{2.93 \times 10^5\ m\mu c}{3.77\ m\mu c/mg \times 10^3\ mg/gm} = 78\ gm$$

which is considerably lower than the 105-gm value given for the standard man. That K's estimated total-body sodium was low cannot be explained on the basis of Na^{24} excretion, since excreta were measured and contained only 1 μc of activity. Part, but not all, of the discrepancy perhaps may be explained by the fact that the neutron dose to the chest and upper portion of the body was higher than to the lower extremities, and compact bone such as the femur is known to have a higher sodium content than highly trabeculated bones such as rib and vertebra.[36] Because of the inequality of dose distribution, the specific activity of nonexchangeable bone sodium in the compact bone of the extremities may have been lower than that of the serum. Again assuming equilibration between serum and tissues sodium specific activity (a reasonable assumption for soft tissues), the total sodium content of the various tissues can be estimated from Table XVI. The estimated values for most tissues are considerably lower than reported in the literature.[37, 38]

Table XVI—Sodium-24 Concentration in Autopsy Specimens (Case K)

Tissue or Organ	Sodium-24 Activity* (mμc/gm)	Tissue Sodium Concentration		Total Sodium-24‡ (μc)
		Estimated (mg/100 gm)	Reported (mg/100 gm†)	
Muscle	1.54	41	65-105	51.65
Skeleton	7.14	190	300	79.08
Blood (whole)	5.31	141	175	31.88
Serum	12.27§	316	300-330	....
Large intestine	3.57	95	160	1.12
Small intestine	5.75	153	160	7.18
Stomach	3.31	88	130	1.03
Liver	2.48	66	120-150	4.84
Lungs	3.62	96	190-240	3.95
Lymphoid tissue	7.94	211	....	6.19
Kidneys	4.36	116	165-220	1.18
Heart	3.57	95	80-160	1.43
Spleen	3.15	84	120	0.37
Adrenals	4.51	120	....	0.06
Thymus	3.28	87	....	0.03
Balance	4.15**	110	....	86.65**
Total-body calculated	3.55	95	...	277
Total-body measured	3.76	110	....	293

*Corrected to time of accident

†References 37, 38

‡Where organ and tissue weights were not available, calculations were made on basis of the standard man[37]

§Corrected for specific gravity of 1.023

**Sodium-24 in balance taken as average of soft tissue analyses.

The estimated Na^{24} content of the skeleton (minus marrow) was 19% of that of the total body, which is considerably lower than the 30% reported by Edelman.[39] Again, the cause of the discrepancy may, at least in part, lie in the inequality of neutron dose distribution.

Miscellaneous Gamma-Ray Spectrometer Measurements

Gamma-ray spectral measurements were made on all excreta, which included urine, feces, and diarrhea fluid passed at the times and in the amounts shown in Table XIII. No gamma activity other than Na^{24} was found in the urine, and the total urinary activity amounted to 0.3 μc. The formed stool passed at 5:20 p.m., 45 minutes after the exposure, contained 0.1 μc Na^{24}. The diarrhea fluid passed 5 minutes later contained 0.5 μc Na^{24} and identifiable amounts of 38-minute Cl^{38}. A third gamma activity was detected also, which corresponded to 2.6-hour Mn^{56}. Manganese-55 has a 13-barn thermal neutron cross section, and the daily intake is normally about 5 mg. The activity found in the diarrhea fluid was believed to have resulted from activation of Mn^{55} in the lumen of the bowel at the time of the accident.

One amalgam filling obtained at autopsy was found to emit gamma rays with energies corresponding to 46-day Hg^{203} and 270-day Ag^{110}. The filling weighed 0.5395 gm and contained 0.1958 gm (36.3%) of silver and 0.2917 gm (54.07%) of mercury.

Phosphorus Analyses of Blood and Urine

Determinations of P^{32} specific activity were carried out on two blood samples and all three urine specimens from K and on five urine specimens from D.

Starting 72 hours after the accident, the beta activity of whole urine and blood plated directly and measured with an end-window Geiger counter was identical with the P^{32} activity as shown by the decay curve, with a half-time of 14.5 days.

Phosphorus was also isolated from a number of samples as reduced phosphomolybdic acid in isobutanol solution by the Berenblum and Chain procedure.[40] A number of the values obtained by evaporating the isobutanol solution to dryness checked well with those from whole dried urine or plasma but in some cases were much lower. Urine samples to which P^{32} was added also gave low results. A possible explanation is that the P^{32} may form volatile phosphate esters during the drying procedure; experiments to test this hypothesis are planned. The data collected by the isobutanol extraction procedure were not used except where results by other methods were lacking.

Analyses for total phosphorus were done by both the Berenblum and Chain and the standard Fiske and Subbarrow methods.[41] Specific activity values, calculated from the counting rates and phosphorus content of serum, red cells, and urine, are given in Table XVII. The specific activity of urinary phosphorus was much greater than that of serum. This observation was first noted by Perley, Langham, and Hoffman[42] in experimental animals and was documented for other criticality accident victims in the report of Hempelmann, Lisco, and Hoffman.[1]

Two possible explanations may be considered: (*A*) About 90% of the phosphorus in the body is in the bones, and because of nonuniformity of neutron dose, etc., it may not have the same average specific activity as the serum and soft tissue phosphorus. Consequently, immediately after exposure, the higher specific activity phosphorus in body fluids and soft tissues may be excreted in the urine before equilibration with less active bone phosphorus could take place. (*B*) The Szilard-Chalmers effect may play a role also, as suggested by Hempelmann et al. If half the P^{32} atoms formed from P^{31} are converted into P^{32+3} ions by recoil, they would presumably form phosphite salts, which may be excreted preferentially by the kidney before being metabolized to phosphates.

The urine samples from D had so little activity that the results from counting small samples were not statistically reliable. Large samples (100 to 200 ml) of all urine specimens except the first were treated with NH_4OH and the alkaline precipitate (free from K^{40}) was

Table XVII—Blood and Urine Inorganic Phosphorus and Phosphorus-32 Determinations (Cases K and D)

Time After Exposure (hr)	Urine Phosphorus		Serum Phosphorus	
	Total (mg %)*	S. A. (mμc/mg P)	Total (mg %)*	S. A. (mμc/mg P)
Case K				
3½	....	....	14†	0.83†
35 (post mortem)	....	....	23	0.16
14	5	152	....	....
17	3	121	....	....
22	42	4.3	....	....
Case D				
4	111	0.03	....	....
16	147	neg.‡	....	....
64	71	neg.‡	....	....

*Normal inorganic phosphorus in urine is 50 to 100 mg %; in serum 3.5 to 5 mg %.

†Phosphorus in red cells run on this sample, total phosphorus 70 mg % (normal 70 mg %), specific activity of cell phosphorus was 0.11 mμc/mg.

‡100 ml of urine showed a count only slightly above background.

Table XVIII—Urinary Phosphorus Specific Activities in Criticality Accident Victims

Case	Sampling Time (hrs)	Specific Activity (mμc/mg P)
1*	17.4	2.97
2	17.4	0.13
3	5.3	9.65†
4	3.1	1.84
6	2.2	0.37
7	1.2	0.51
8	2.2	0.07
9	1.2	0.04
10	2.2	0.04
D	4	0.03
K	14	152†

*Case numbers refer to Hempelmann.[1]

†Serum phosphorus specific activity was measurable only in Case 3 (0.35 mμc/mg) and Case K (0.82 mμc/mg), both of which terminated fatally.

counted. The results indicated negligible activity.

A comparison of the urine phosphorus specific activity of K and D with that of other criticality accident victims at Los Alamos is shown in Table XVIII. These data merely emphasize the apparent lack of any significance of urinary and serum phosphorus specific activity measurements with regard to evaluation of criticality accidents. It is interesting but puzzling that the P^{32} concentration (P^{32}/ml) in K's urine appeared to decrease exponentially, with a half-time of ~4 hours.

Neutron-Induced Phosphorus-32 in Sulfur-Rich Tissues (Case K)

Tissues with a high sulfur-to-phosphorus ratio afford the possibility of estimating the fraction of neutron dose resulting from neutrons with energies in excess of 2.5 mev by determining the P^{32} produced by the $S^{32}(n,p)P^{32}$ reaction. Samples of hair, xiphoid cartilage, and testis were wet-ashed with nitric acid, and aliquots of the digests were used for total phosphorus,[40, 41] sulfur,[43] and P^{32} determinations. The method of Berenblum and Chain[40] was found to be particularly useful for separation of P^{32} and Na^{24} activities. Results of these measurements are summarized in Table XIX. Application of the data to the estimation of incident fast neutron dose and dose distribution is shown in Section VI. Fingernails and toenails could be used also to estimate incident fast neutron dose to the extremities, but samples of these tissues unfortunately were not obtained.

Plutonium Analyses of Tissues (Case K)

The victim of this fatal accident had spent a total of approximately 6 years of an 11½ year employment period working as a plutonium process operator. Because of his long potential exposure to this material, tissue samples were obtained at autopsy and analyzed for Pu^{239}. Since death resulted from an overdose of radiation involving no plutonium contamination, the conditions of the accident did not influence the plutonium content found in his tissues and organs.

Table XIX—Fast Neutron-Induced Phosphorus-32 Activity in Sulfur-Rich Biological Materials (Case K)

Material	mg P/g	mg S/g	P/S Ratio	Phosphorus-32 d/m/mg S (t = 0)	Calc. Dose (rads)
Hair	0.063	45.50	0.001	24.0	2600
Xiphoid cartilage	0.260	9.26	0.028	31.0	3000
Testis	1.900	17.90	0.160	Background	....

Table XX—Employment History of Case K

Period	Occupation	Time (days)
6/17/46 to 1/24/49	Pu^{239} recovery operator	947*
1/24/49 to 6/4/54	U^{235} recovery operator	1,987
6/4/54 to 6/8/55	Resigned—no exposure	369
6/8/55 to 12/31/58	Pu^{239} recovery operator	1,297*
Total plutonium exposure time		2,244

*Between first and second plutonium exposure periods, exposure conditions had been greatly improved.

These data are of interest because they provide for the first time limited information on *(a)* the efficacy of industrial hygiene and engineering practices in plutonium-processing operations; *(b)* body distribution of plutonium in an individual exposed primarily by inhalation to low-level plutonium aerosols over a prolonged period; and *(c)* reliability of estimates of body burden from urinary excretion data when exposure has been primarily via inhalation.

Plutonium Exposure—K's employment and job assignment history is shown in Table XX. During the first period of plutonium exposure (6/17/46 to 1/24/49), his work consisted of chemical processing involving plutonium nitrate solutions, plutonium oxalate, and occasionally plutonium fluorides. During the second period (6/8/55 to 12/31/58), his work consisted largely of liquid-liquid extraction of plutonium under greatly improved exposure conditions.

Detailed exposure records were kept during the periods when the employee was working with plutonium. These records included plutonium air concentrations in the processing rooms; the operator's nose swipe counts done several times a week up to the end of 1955, and frequently but irregularly thereafter; daily hand counts; and frequent plutonium assays of 24-hour urine specimens. Average plutonium

Table XXI—Average Concentration of Air-Borne Plutonium in Areas in Which K Was Assigned

Year	Room 308 (d/m/M³)	Room 313 (d/m/M³)	Room 308 (d/m/M³)	Room 413 (d/m/M³)	Rooms 212, 213, 218 (d/m/M³)
1946	6	16	188	15	
1947	11	25	77	98	
1948	Not used	24	35	69	
1949	Not used	19	30	72	
1949-1954	Worked with enriched uranium				
1955					3
1956					3
1957					4
1958					4

*Table XXII—Record of High Nose Swipe Counts**

Date	Right/Left Nostril (c/m)
1946 7/29	189/320
7/30	87/70
9/5	149/19
9/25	55/4
11/1	61/15
12/10	57/68
12/30	164/106
1947 1/21	102/61
4/1	91/135
7/7	144/40
10/3	120/78
1948 2/10	0/59
4/26	86/3
6/9	33/50
6/10	244/72
7/2	72/1
8/2	65/0
12/1	50/38
After 1948	None

*Technique consisted of rotating a piece of dampened filter paper on an applicator in each nostril, after which the paper was unrolled, flattened, dried and counted. Fifty counts per minute was arbitrarily taken as the limit of significance.

air concentrations to which the individual was exposed are presented in Table XXI. The instances when his nose swipe counts went above 50 c/m (arbitrarily chosen as the limit of significance) are listed in Table XXII, and his urine assay record is given in Table XXIII. No tabulation of hand counts is given, since they were without exception below significant levels. Results of fecal analyses were not available. Because of the analytical and sampling difficulties involved, fecal analyses are not a routine practice at the Los Alamos Scientific Laboratory.

There were no specific accidents to which the individual's exposure could be attributed. However, as might be expected, a number of minor mishaps occurred during the period of employment. The detailed record of such minor incidents is summarized in Table XXIV.

Plutonium in Tissues and Organs—At the time of autopsy, tissues were taken specifically for plutonium assay. The specimens taken and their plutonium content are shown in Table XXV. The assays were carried out using the alpha-track counting method.[44] Two independent analyses of aliquots from each tissue sample, ribs, sternum, vertebrae, lungs, liver and lymph nodes, were made by the analytical section of the Los Alamos Industrial Hygiene Group and also at the Hanford Atomic Products Operation,* where they were analyzed independently by both the Biological Laboratory and the Bioassay Group. The values given in Table XXV are averages and standard deviations for the

*We wish to express our appreciation to our colleagues of the Biology Laboratory and Bioassay Group of the Hanford Atomic Products Operation for cooperation in supplying independent analyses of the tissue samples.

Table XXIII—Results of Periodic Plutonium Urine Assays for Entire Period of K's Employment

Date	d/m/24-hr Specimen	Date	d/m/24-hr Specimen
1946 8/9	1.2	1955 8/1	1.2
9/19	4.7	8/12	0.6
12/18	1.7	8/19	0.0
1947 4/18	0.7	9/30	0.7
5/23	0.7	11/14	0.7
6/26	0.7	12/27	0.6
7/30	0.0	1956 2/9	0.0
8/27	1.0	4/5	0.7
10/2	1.5	4/30	0.0
11/7	0.8	6/8	0.4
12/8	4.0	7/20	0.6
1948 1/13	1.0	8/23	0.5
2/13	0.0	9/25	0.0
3/19	0.0	10/24	0.0
4/22	2.0	11/23	0.0
6/23	3.7	12/17	0.1
7/22	0.0	1957 1/31	0.23
8/19	0.8	2/28	0.68
9/20	3.0	4/12	0.22
10/26	2.0	5/14	0.12
11/22	2.5	6/14	0.11
12/21	0.0	7/15	0.03
1949 1/24	Uranium	8/19	0.00
1/31	2.0	9/20	0.20
7/14	1.2	10/22	0.21
1950 2/8	0.8	10/31	0.39
9/1	0.1	11/14	0.51
1951 2/28	0.8	1958 1/10	0.00
9/4	0.7	2/21	0.65
1952 5/19	0.3	3/25	0.51
12/14	0.0	5/7	0.25
1953 9/4	0.0	6/19	0.55
1958 9/4	Off uranium	7/30	0.49
6/18	0.0	9/15	0.79
1955 6/8	Back on plutonium	11/28	0.47

Table XXIV—Summary of Minor Exposure Incidents of Case K during Period of Employment

Date	Type of Incident	Potential Exposure
8/26/46	Minor laceration on thumb	No alpha activity detected
12/30/46	Helped clean up spill of plutonium solution	Air concentration 52 d/m/M^3 for 8-hr day; nose count 164/106 d/m
4/22/47	Received nitric acid burns on arm	No record of contamination
9/3/47	Small cut on hand, received while making material transfer	No alpha activity detected
12/14/47	Puncture wound on right hand from a screw point on an instrument panel	No contamination reported
3/17/49	Helped clean up spill of enriched uranium	No air concentration or nose swipe data recorded
4/22/50	Exposed to fumes of oxides of nitrogen	No contamination involved
8/10/53	Helped clean up spill of enriched uranium	Room air concentration 8 d/m/M^3; nose count 4 d/m
8/9/55	While adding caustic to a plutonium and americium solution, materials sprayed out of reaction vessel; operator was wearing face shield and respirator	No body contamination detected; nose count 22/28 d/m; room air concentration 75 d/m/M^3
11/25/58	Maintenance work involving removal of plutonium-contaminated insulation from an evaporator-condenser	Nose swipe count 0 d/m; room air concentration 1070 d/m/M^3; operator was wearing Wilson 800 respirator

four independent analyses. The standard deviation for the lymph nodes includes variation in sample, as well as variation in analysis, since different lymph node samples were used in the independent determinations. The highest plutonium concentration was found in the pulmonary lymph nodes (125 ± 57 d/m/gm), followed by the liver (9.9 ± 1.4 d/m/gm), lungs (4.8 ± 0.6 d/m/gm), and then vertebrae (2.1 ± 0.6 d/m/gm). The average of all bone samples was 1.4 ± 0.7 d/m/gm, for which the standard deviation includes the variation among the different bone samples plus the analytical variation.

The total organ and body content, calculated from the data in Table XXV, are shown in Table XXVI. The estimated total body burden was 0.018 μc.

As a result of changes in production methods, the Pu^{238}/Pu^{239} ratio of plutonium processed at the Laboratory increased considerably between 1946 to 1948 and 1955 to 1958. Determination of the Pu^{238}/Pu^{239} ratios in bone, lymph node, liver, and lung samples indicated bone and lymph nodes had the lowest ratio (corresponding generally to material produced in 1946 to 1948), and lung samples had the highest (corresponding roughly to more recently produced material). The Pu^{238}/Pu^{239} ratio in the liver was intermediate.

Discussion—The data in Tables XXI and XXII show that all high plutonium air concentrations to which the employee was exposed and all high nose swipe counts recorded

Table XXV—Plutonium Concentration in Autopsy Samples (Based on Actual Analytical Data)

Organ or Tissue	Gross Weight at Autopsy (gm)	Plutonium Concentration (d/m/gm wet wt.)
Psoas muscle	....	0.01
Kidneys	270	0.05
Heart	400	0.06
Cartilage	....	0.14
Spleen	116	0.18
Sternum	....	1.0 ± 0.2
Ribs	....	1.2 ± 0.3
Vertebrae	....	2.1 ± 0.6
Lungs (minus major bronchii)	850	4.8 ± 0.6
Liver	1,950	9.9 ± 1.4
Bronchial lymph nodes		125 ± 57*

*Includes variation in different lymph node samples, as well as analytical variation.

occurred during his earlier period of exposure. It is very likely that most of his plutonium burden was accumulated during this period. The record summarized in Table XXIV shows that there were no specific incidents to which his plutonium exposure could be attributed. The summary is given principally to point out that close attention was given to all potential modes of exposure and thereby to emphasize the certainty with which a contaminating accident can be ruled out as the source of the subject's plutonium burden. It is most likely that the body burden, in this case, resulted from chronic inhalation exposure over a long period to a low-level plutonium-contaminated atmosphere. The

above speculations regarding time and mode of exposure are supported also by the indication that the Pu^{238}/Pu^{239} ratio in lymph nodes and bone appeared to correspond to that of plutonium being processed during the early period of the subject's exposure.

Three different urine assay procedures were used during the 12-year period over which the urine data shown in Table XXIII were collected. Each change resulted in somewhat greater reliability of the data. In 1957, the Hanford alpha-track counting procedure was adopted.[44] Urine assays from this time on have considerably higher reliability than previously. Even during 1957 and 1958, however, there was considerable variation in the assays, which is probably due both to analytical limitations and to normal physiological fluctuations. The employee's systemic plutonium burden was estimated from the urine assays using empirical equations derived from human excretion data.[45] Following an acute exposure occurring at known time, the retained plutonium body burden (D_R) is given by the expression

$$D_R = 435\ Ut^{0.76} \qquad (1)$$

in which U is the plutonium (c/m, d/m, μc) in a 24-hour urine sample collected days after the time of exposure. D_R is given in the same units used to express U. Since this equation is applicable to relatively acute exposure occurring at known time, it is necessary in protracted exposure cases to assume an effective time of exposure which, to a first approximation, may be taken as the midpoint of the work period. Following chronic invariant exposure to plutonium, the total systemic intake (D_t) is given by the expression

$$D_t = \frac{130 \times m \times U}{(n + \frac{1}{2})^{0.26} - (n - m + \frac{1}{2})^{0.26}} \qquad (2)$$

in which m is the duration of exposure (days), and U is the average d/m/24-hour urine sample taken n days from the beginning of exposure. D_t is the systemic exposure and it is necessary to subtract the amount excreted in order to obtain the amount retained (D_R). However, since only about 10% of a plutonium burden is excreted in 10 years,[45] such a correction is insignificant in most cases. The above expressions indicate the determination of body burden from a single 24-hour urine assay. Analytical limitations of the assay methods and normal physiological variations in urinary plutonium excretion make such estimates completely unreliable, and in practice it is better to use the average of several consecutive assays (even though they may be weeks or months apart).

Because of the nature of the exposure, neither of the above equations is specifically applicable to the case under consideration. Application of Equations 1 and 2 to the average of all urine assays run during 1949 to 1951 (during which time there was no exposure to plutonium) gives 0.033 and 0.031 μc, respectively, for the employee's body burden at that time as a result of his first period of exposure. During 1957 and 1958, frequent urine assays were run using the more sensitive and reliable alpha-track counting method. Estimations based on Equations 1 and 2 (assuming all his exposure occurred during the earlier work period, and using the average of the 1957 and 1958 urine assays) gave 0.034 and 0.031 μc, respectively, for the body burden at the time of death. The latter estimates may be high, since they are predicated on the assumption that the entire body burden was accumulated during the earlier work period and that exposure during the second period made no contribution to the 1957 and 1958 average urine assay value. That this assumption is approximately correct is borne out by the estimates of burden at the end of the employee's first period of exposure. A method of estimating plutonium body burden employing IBM 704 Fortran programming of all urine assay data has been developed by Lawrence.[46] His estimate of the subject's body burden at time of death was 0.019 μc. The burden derived from tissue analyses (Tables XXV and XXVI) was 0.018 μc, which is 45% of the maximum permissible level of 0.04 μc.[47]

The above agreement between body burden from tissue analyses and estimated burden from urine assays is so very satisfactory that it is undoubtedly fortuitous. Determination of body burden from tissue analyses is subject to considerable sampling uncertainty. Since it is not possible to analyze the entire body, it is neces-

Table XXVI—Total Body Burden Estimated from Tissue or Organ Weight and Plutonium Content

Organ or Tissue	Weight (gm)	Total Content (d/m)
Liver	1,950	1.930×10^4
Skeleton (average)	10,000	1.400×10^4
Lungs (minus bronchii)	850	0.408×10^4
Pulmonary lymph nodes	10	0.125×10^4
Muscle	30,000	0.030×10^4
Heart	400	0.002×10^4
Spleen	116	0.002×10^4
Kidneys	270	0.001×10^4
Remaining tissues*	26,400	0.026×10^4
Total	70,000	3.924×10^4 (0.018 μc)

*Assuming plutonium content of the remaining tissues is the same as that of muscle.[45]

sary to analyze aliquots of the various organs and, on the assumption of uniform distribution and representative sampling, calculate the total body content from the organ weights. This assumption is particularly uncertain with regard to the skeleton, as shown by the analytical data for sternum, ribs, and vertebrae (Table XXV).

Some uncertainty in the body burden estimated from urine assays may be expected also from the uncertainty in the exponents of the time parameters in Equations 1 and 2. When t = 10 days, a 10% error in the exponent of t (Equation 1) would make an 18% error in the body burden estimated from the urine assay. The error would increase with time, approaching a factor of about 2 at t = 3,500 days. Indication that the exponent of t in the basic urinary excretion equation[45] may be in error (by about 10%) in the direction resulting in overestimation of the body burden was obtained recently by reestimation of the plutonium burdens of workers exposed at the Laboratory during 1944 and 1945 who had received no subsequent exposure. When estimated from a urine sample collected approximately 10 years after termination, their systemic burdens were, in most cases, about a factor of 2 higher than the estimates based on urine samples collected during or immediately after exposure. Most of the cases, however, were believed to be inhalation exposures, and it is possible, although seemingly unlikely, that their systemic burdens did increase as a result of absorption of plutonium deposited in the lungs and lymph nodes.

The distribution of plutonium in the various tissues and organs was somewhat surprising. Approximately 50% of the body burden was found in the liver and 36% in the skeleton (Table XXVI). One hundred fifty days after intravenous injection of Pu^{+4}-citrate in man, approximately 65% of the administered dose was found in the skeleton and 22% in the liver.[48] Rat experiments show that the relative concentration of plutonium in bone and liver following intravenous injection is dependent on the chemical form and valence state of the material administered.[49] It is quite possible, in the present case, that the partitioning of plutonium between the liver and skeleton was influenced both by the chemical or physical nature of the plutonium and by the route of exposure. The respiratory route of exposure was undoubtedly responsible for the high plutonium concentrations found in the lungs and pulmonary lymph nodes.

Some interesting qualitative speculations regarding relative deposition and clearance rates of plutonium in various tissues may be drawn from the Pu^{238}/Pu^{239} ratios in bone, lymph nodes, liver, and the lungs. The Pu^{238}/Pu^{239} ratios of the plutonium deposited in bone and lymph nodes appeared to correspond with that of plutonium produced in 1946 to 1948 (which was the subject's earlier and greater period of exposure). The Pu^{238}/Pu^{239} ratio of the material deposited in the lungs, however, appeared to correspond to that of more recent production. The above observations suggest (*a*) a relatively rapid clearance rate for plutonium in the lungs compared to that in bone and lymph nodes, and (*b*) that a relatively small percentage of the material deposited in the lungs must migrate to these tissues. Since the Pu^{238}/Pu^{239} ratio of material in the liver was intermediate between that deposited in the bone and lymph nodes and that in the lungs, the rate of clearance from the lungs to the liver must be relatively fast and the retention time in the liver must be longer than in the lungs.

The biologically effective dose rate to the various tissues of the subject may be estimated from the observed plutonium concentrations (Table XXV) and the following expression derived from the Recommendations of the International Commission on Radiological Protection[50]:

$$R = \frac{C \times \Sigma E(RBE)n}{2.8 \times 10^{-3}}$$

In this expression, R is the dose rate in rem per week, C is the plutonium concentration in μc per gm, and $\Sigma E(RBE)n$ is an effective energy term weighted for the RBE of alpha particles and the nonhomogeneity of energy distribution and absorption in the tissue. The weighted energy terms for plutonium in soft tissue and bone are 53 and 270, respectively. Calculated in the above manner, the pulmonary lymph nodes were subject to the highest biologically effective dose rate (—1 rem per week), the liver next (0.08 rem per week), followed by the bone and lungs (0.06 and 0.04 rem per week, respectively). The estimated alpha radiation dose to the lymph nodes may be considerably too high because of their shrinkage in mass as a result of the acute radiation dose (—10,000 rads of fast neutrons plus gamma rays incident to the chest) received during the criticality accident.

No definitive conclusions can be drawn from a single case, but these observations again bring up the troublesome questions of choice of the critical organ following chronic inhalation exposure, the size of the critical tissue volume, and the relative sensitivity of various tissues to chronic radiation damage.

SECTION VI

Dosimetric Calculations

Payne S. Harris, M.D.

THERE were a number of complications connected with evaluation of doses to personnel involved in the accident. These ranged from the geometric and moderator characteristics of the source to the movement of personnel in the vicinity of the source after the accident. As has been usual in these situations, the standard dosimeter coverage was inadequate and, in some cases, absent.

The personnel involved can be considered in two groups. One group consists of those intimately associated with the accident and includes only three individuals, K, D, and R. This portion of the dosimetry report is concerned only with the exposures of these three persons. They received the highest and most significant doses. The second group consists of all other individuals who were in the area at the time of the accident and those who entered it afterward. The estimates of doses received by the personnel in the second group are given in Section VII.

Physical Characteristics of the Source

The critical reaction occurred in a 225-gal stainless steel tank containing approximately 130 gal of material. A schematic diagram of the tank is shown in Fig. 8. The critical reaction occurred in the upper layer of solution (labeled solvent). There was 3.27 kg of plutonium dissolved in this layer of organic solvent, which consisted of a tributyl phosphate-kerosene mixture. The aqueous phase below contained only 40 gm of plutonium, while the total solids ("heel," etc.) contained only 60 gm. Apparently, when the stirrer was started, the material in the organic phase was brought into a critical configuration in the horizontal center of the tank slightly below the center of the organic layer. The geometric level of the critical reaction was determined by linear measurement of the long-lived induced gamma activity in a stainless steel baffle located inside the tank.

There was apparently enough heating by the reaction and dispersal by continued stirrer operation to prevent any oscillation of the system such as occurred in the Oak Ridge accident.[51] Thus the whole event consisted of a single supercritical reaction. The total fissions that occurred were determined subsequently by standard radiochemical analysis and found to be $\sim 1.5 \times 10^{17}$. Under these conditions, the pulse width was probably less than 200 μsec. This undoubtedly caused a rapid temperature increase in the solution, which in this time period would cause quite a thermal shock. The tank, in fact, was found to have moved $\frac{3}{8}$ in. on one of its supports.

The general position of a chemical operator in performing the standard operation is indicated by the posed photograph shown in Fig. 1 and in Fig. 8. A number of operators were questioned and demonstrated this standard technique. The schematic outline shown in Fig. 8 gives the most likely dimensions, distances, and conditions prevailing at the time of the accident. In no case during demonstration of the technique was the frontal plane of an operator's body found to be closer than 6 in to the tank. Thus thermal shock could not be transmitted directly to the chest, abdomen, etc. From the dimensions shown in Fig. 8, it can be seen that the area of the xiphoid was actually closer to the essentially unmoderated critical reaction center than any other portion of the body. Also, the geometry was such that inverse square could materially change the dose by a factor of 2 over the average body thickness of 30 cm without any consideration of absorption. Finally, it can be seen that the moderator mass varied from essentially zero to greater than 70 cm of H_2O over the exposure profile. These considerations certainly made the dose distribution of both neutrons and gamma rays completely anisotropic as far as the operator K was concerned. It is, therefore, possible to consider only average dose to the body and incident dose to specific areas.

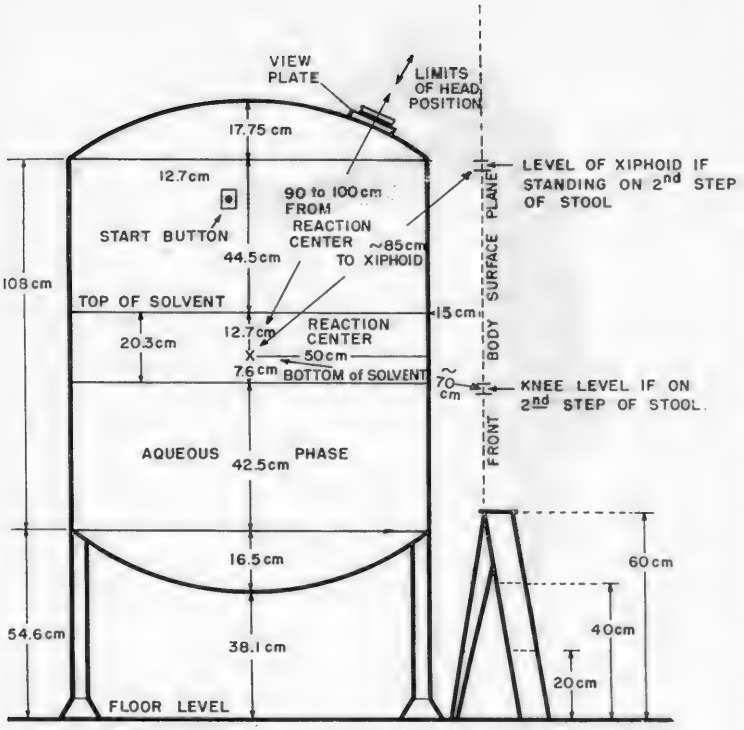


Fig. 8—Schematic diagram of solvent-treatment tank set-up.

Neutron Dose

The neutron dose to the operator K is of primary interest. This portion of his total exposure was due almost exclusively to fast rather than thermal neutrons. The incident neutron dose may be expected to vary from point to point because of position with respect to the source and the varying thickness of moderator. The depth dose may be expected to vary also with respect to both geometry and absorption.

Several measurements were available from which the fast neutron component of K's dose could be estimated. These included measurements of blood and total body Na^{24} activity (see Section V), serum sodium specific activity, induced activity in materials in his pockets or clothing, and specific induced activities in selected tissues. The applicability of all such measurements to neutron dose estimation is predicated on the assumption that thermal neutrons did not cause an appreciable amount of the total activity measured. This assumption seems justified on the basis that the thermal neutron fluxes were low or that the activation cross sections were small, or a combination of the two.

If one accepts the above assumption, two uncertainties remain in the estimation of fast neutron dose from Na^{24} measurements. One is the estimation of the total amount of Na^{23} (fixed plus exchangeable) in the body. Surprisingly, this is not well known, although 105 gm is the value given for the standard 70-kg man.[50] Total-body activity measurements apply to total-body sodium, whereas specific activity measurements of blood or serum sodium apply primarily to the exchangeable fraction. The second uncertainty is the variation in induced Na^{24} activity per unit of neutron dose as a function of source spectrum change. It has been postulated[51] that the activity per unit dose is a slowly changing function of spectrum. This assumption implies that the mass and moderating ability of the irradiated object are enough to wipe out any significant spectral effect.

An experiment was performed using a Los Alamos prompt critical assembly (Godiva II) as a fission neutron source to check the second uncertainty. Varying thicknesses of polyethylene moderator were interposed between the source and a point of measurement, and the neutron dose was measured. Afterward, an 18-liter polyethylene jug filled with a 1.29% $NaHCO_3$ solution in water was positioned at the same point and the induced Na^{24} activity measured as a function of moderator thickness. The results of the measurements are shown in Table XXVII and indicate that the induced activity per unit of neutron dose is not a strong function of spectral degradation under these conditions of exposure. Induced Na^{24} measurements can be used, therefore, to estimate the average fast neutron dose to the exposed subjects.

Estimation of Average Fast Neutron Dose—The total-body sodium activities can be used to estimate the average fast neutron dose by comparison with the burro experiments carried out in connection with the Oak Ridge National Laboratory's Y-12 criticality accident.[51] In these experiments, a burro was exposed to 48 rads of fission neutrons and induced Na^{24} activity measurements carried out. Assuming the sodium concentration in the human is the same as that in the burro (comparison of blood concentrations indicate that this assumption is reasonable), the average total-body fast neutron dose may be estimated from total body

Na^{24} measurements using the following expression

$$Rad_S\ (ave) = \frac{Act_S}{Act_B} \times Rad_B$$

where Act_S = activity in the subject in $\mu c/kg$; Act_B = activity in the burro in $\mu c/kg$; Rad_B = dose to the burro; and Rad_S is the dose to the subject. The Na^{24} activity in the burro was found to be 0.236 $\mu c/kg$, following a total neutron dose of 48 rads. In a similar manner, the average fast neutron dose to the exposed subjects can be estimated from blood Na^{24} activity and specific activity of the serum sodium. The burro exposed to 48 rads had a blood Na^{24} activity of 0.29 $m\mu c/ml$ and a serum sodium specific activity of 0.187 $m\mu c/mg$ (assuming a 50% hematocrit).

Average fast neutron doses, estimated from the various Na^{24} measurements, are shown in Table XXVIII. The values for K's average body dose range from 835 to 968 rads.

The average fast neutron dose to K can be estimated also from the Godiva II experimental data (Table XXVII) using the Na^{24} values obtained for the 18-liter water phantom containing 1.29% $NaHCO_3$. With 6 to 9 in of moderator between the fission neutron source and the phantom, the induced Na^{24} activity was approximately 100 c/m/rad. Under this set of circumstances, the initial counting rate of the phantom was 5.575×10^3 c/m, with a dose of 57.1 rads. Calibration of the counting equipment indicated a sensitivity of 1.923×10^{-3} $\mu c/c/m$. Thus, the total activity induced in the phantom was 10.7 μc. The sodium concentration in the phantom was 3.53 gm/liter, while the value given for man[50] is 1.5 gm/kg, or 1.5 gm/liter based on a density of unity. K's total body Na^{24} activity was 293 $\mu c/kg$. The induced Na^{24} activity of the phantom was 10.7 $\mu c/18$ kg = 0.595 $\mu c/kg$. From these values, K's average neutron dose is estimated as

$$\frac{4.10}{0.595} \times \frac{3.53}{1.5} \times 57.1 = 926 \text{ rads}$$

which agrees satisfactorily with the doses estimated from total body and blood Na^{24} measurements and the serum sodium specific activity. Since there is no unequivocal reason for assuming that any one of the above estimates is more accurate than the others. K's average total body fast neutron dose is assumed to be the average of all the estimates, or ~900 rads. His tissue dose, however, definitely was not uniform and varied both with depth and with respect to moderator characteristics and geometry of the source.

Estimation of Incident Fast Neutron Dose—Estimates of fast neutron dose incident on different regions of K's body were made using other measurements. Samples of hair (which has a high sulfur content) were obtained, and the P^{32} activity produced by the $S^{32}(n,p)P^{32}$ reaction was measured. This is a threshold reaction for neutrons with energies greater than 2.5 to 3 mev. For a fission spectrum, the cross section is 0.230 barn; the cross section is about the same as that for the $P^{31}(n,\gamma)P^{32}$ produced by thermal neutrons. In hair, however, there is less than 1% as much phosphorus as sulfur present, and thermal neutron production of P^{32} from P^{31} may be neglected. The sulfur concentration in K's hair was found to be 45.6 mg/gm, and the P^{32} activity was 27 d/m/mg of sulfur. The fast neutron flux incident to the head was estimated from the relation

$$N = N^*/\lambda = \phi \frac{\sigma f A}{W}$$

or

$$\phi_S = \frac{N^* W}{\lambda \sigma f A}$$

where N^* = activity per gram of hair = 20.5 d/sec/gm; W = atomic weight of sulfur = 32; λ = decay constant for $P^{32} = 5.65 \times 10^{-7}$ sec^{-1}; σ = activation cross section = 0.230×10^{-24} cm^2; f = fractional concentration of sulfur in hair by weight = 0.0456; A = Avogadro's number = 6.02×10^{23} atoms; and ϕ_S = total fast

Table XXVII—Effect of Thickness of Moderator on Induced Sodium-24 in $NaHCO_3$ Water Solution

CH_2 Thickness (in.)	Sodium-24 (c/m/rad)
0	80
3	80
6	100
9	100

Table XXVIII—Average Total-Body Fast Neutron Dose from Body and Blood Sodium-24 Concentration and Serum Sodium Specific Activity

Subject	Body Sodium-24 ($\mu c/kg$)	Blood Sodium-24 ($m\mu c/ml$)	Serum Na S.A. ($m\mu c/mg$)	Dose Estimates: Body Sodium-24 (rads)*	Dose Estimates: Blood Sodium-24 (rads) †	Dose Estimates: Serum Na S.A. (rads)
K	4.10	5.3	3.77	835	880	968
D	0.014	0.016	0.01	2.8	2.6	2.6
R	0.007	....	....	1.4	....	....

*Assuming total body sodium concentration in man and the burro is the same.

†Assuming the blood sodium concentration in man and the burro is the same.

neutron flux seen by sulfur (n/cm²). Thus

$$\phi_S = \frac{20.5 \times 32}{(5.65 \times 10^{-7}) \times (0.230 \times 10^{-24}) \times 0.0456 \times (6.02 \times 10^{23})} = 1.78 \times 10^{11} \text{ n/cm}^2$$

The flux-to-dose conversion factor for neutrons above the sulfur threshold is 3.63×10^{-9} rad/n/cm², giving a dose estimate of ~650 rads incident to the region of K's head. With the source as indicated in Fig. 8, the total neutron flux in the head direction was essentially an undegraded fission spectrum. Under these conditions, a comparison with Godiva II measurements indicates that neutrons above the sulfur threshold deliver approximately 25% of the total neutron dose. The total fission neutron dose incident to the head was, therefore, about 2,600 rads. Extrapolation of neutron dose measurements performed with the Godiva II assembly indicates 1.5×10^{17} fissions would deliver a dose of 3,700 rads at a distance of approximately 100 cm from the source, the distance assumed in Fig. 8 as the most probable position of K's head during performance of the stirrer operation. Although the two estimates differ appreciably, it is not surprising since the position of the head was not known. For this reason, the estimate from the P^{32} measurement is considered the more likely value.

Consideration of the distances and source characteristics shown in Fig. 8 suggests that the upper abdomen in the region of the xiphoid cartilage probably received the maximum incident neutron dose. Although other regions of the body were closer, the amount of moderator between the source and body surface probably resulted in a considerably lower dose. A sample of K's xiphoid cartilage was analyzed also for sulfur, phosphorus, and P^{32}, and the results used to estimate incident fast neutron dose to this region of the body. The phosphorus-to-sulfur ratio was 0.028, and phosphorus capture of thermal neutrons could again be neglected.

The P^{32} activity was 4.7 d/sec/gm, and the sulfur fraction by weight was 0.00926. The incident neutron flux (ϕ_S), calculated in the manner shown previously, was 2.05×10^{11} n/cm². Using the same conversion factors and assumptions used previously, the incident fast neutron dose to K's upper abdominal area is estimated at about 3,000 rads. Extrapolation of neutron dose data from the Godiva II assembly gives an estimate of ~5,000 rads from 1.5×10^{17} fissions at the distance of the xiphoid (Fig. 8). The agreement between the two estimates is considered satisfactory when the uncertainty in K's position, the increasing amount of moderator between the source and surface, and the differences in the two sources are considered. The increasing amount of moderator would tend to decrease the fraction of dose due to neutrons above the sulfur threshold.

A sample of testicular tissue was analyzed also, but the P^{32} activity was below the level of detection. Failure to detect P^{32} in the testis supports the conclusion that moderation of the source spectrum by intervening water occurred with degradation of high energy neutrons to below the sulfur threshold. It may be concluded also that a significant absorption of thermal neutrons occurred, since the phosphorus-to-sulfur ratio in the testis was 0.11.

Metal buttons were removed from the coveralls worn by K at the time of the accident, and their induced activity was measured. The radiation emitted was identified as the annihilation radiation from Cu^{64}. Unfortunately, the buttons (which varied in activity by a factor of ~1.7) were not labeled as to location on the coveralls as they were removed. The activity of the various buttons, corrected to time of accident is shown in Table XXIX. Calibration of similar buttons taken from the same type of coverall was attempted during the Godiva experiments, designed to study the effect of moderator on induced Na^{24} activity in the 18-liter water-$NaHCO_3$ phantom. The activity induced in the buttons resulted from thermal neutron capture. However, a free-air measurement with Godiva II indicated that the thermal neutrons from Godiva itself could be neglected. When the buttons were activated on the front of the phantom with 3, 6, and 9 in of polyethylene moderator between the source and the buttons, the measurements indicated an essentially constant ratio of 0.17 rad/c/m. The incident neutron dose indicated by each button is shown in Table XXIX. These results show a variation of from 1,500 to 2,500 rads and are not inconsistent with the neutron dose consideration given previously.

Table XXIX—Cu^{64} Activity of Buttons from Coveralls Worn by K (corrected to time of accident)

Button Number*	Activity (c/m)	Incident Neutron Dose (rads)
1	11,100	1,900
2	13,500	2,300
3	11,300	1,900
4	9,800	1,700
5	8,730	1,500
6	14,500	2,500
7	9,480	1,600
Average	11,200	1,900

Position on coveralls not known

Gamma-Ray Dose

In many respects, estimation of K's gamma-ray exposure was more difficult than the estimation of neutron dose. Gamma doses to D and R were reasonably well known, since both were wearing film badges, but no film badge results were available for K, and the nature and geometry of the source were important in the estimation of his gamma dose by other means. The gamma-to-neutron dose ratio would be expected to vary from point to point because of the moderating conditions. Three different components contributed to the total gamma-ray dose. First was fission gamma rays; second, the dose due to capture gamma rays from the hydrogen in the moderator; and, third, that due to residual fission products and induced activities in the tank and its contents. As far as K was concerned, the third portion may be neglected. D and R (as will be seen later) received a major portion of their gamma-ray exposure from the residual fission products and associated activities.

Estimates of the gamma-to-neutron dose ratio in the area occupied by K may be made from the results of the Oak Ridge National Laboratory's mock-up experiment following the Y-12 accident.[51] These experiments indicated a dose ratio of approximately 3. Although a value of 3 may roughly apply to the upper portion of K's body, it certainly would not apply to the lower portion in the directions of large thicknesses of hydrogenous moderator. In the presence of significant amounts of hydrogenous moderator, the gamma-to-neutron ratio increases rather rapidly owing to hydrogen capture gamma rays.[52] Neglecting fission gamma rays, the capture gamma-to-neutron dose ratio increases rapidly from 0.5 at 20 cm of water shielding to 5 at 50 cm, and 20 at 100 cm. Application of these observations to the distances and source conditions shown in Fig. 8 suggests that the incident gamma-to-neutron dose ratio over K's body may have varied from 3 to 1 at the head and xiphoid region to 10 to 1 at the feet. In the regions of high ratios, however, the neutron dose was very significantly decreased owing to fast neutron moderation. Experiments indicate that the fast neutron dose relaxation length[63] is of the order of 10 cm in a water shield. Some build-up close to the source occurs, but one would estimate that the actual fast neutron incident dose to the lower portion of K's body was only a few per cent of the unmoderated value in the region of the head and xiphoid shown by the sulfur measurements. Therefore, even though the gamma dose to the lower portions of the body may have been 10 times as great as the neutron dose, the total dose to this area was undoubtedly only a fraction of that to the upper portions. From these purely theoretical considerations, an estimate of 3,000 to 4,000 rads as K's average total-body gamma-ray dose seems reasonable.

Table XXX—Transmission Data for Co^{60} Gamma Rays

Position	Dose Rate (mr/hr)*	Transmission Factor
Film badge rack	1.86	7.0×10^{-6}
R's station	4.23	1.6×10^{-5}
D's station	5.64	2.1×10^{-5}

*Ionization chamber readings from 20-curie source placed near the solvent-treating tank.

Located in a rack 137 ft from the center of the criticality excursion were 46 previously unexposed film badges. After the accident, these films showed an average gamma-ray exposure of 670 ± 90 mr. Calculations showed that only about 4% of the dose indicated by the film badges could have resulted from residual fission product gamma-ray exposure, which certainly constituted a negligible fraction of K's dose.

An experiment was carried out to measure gamma-ray transmission from the source to the film badge rack before the general geometric features of the area were disturbed; only the contents of the solvent-treating tank had been transferred. Using a Co^{60} source of approximately 20 curies placed at about 6 in from the outer wall of the solvent tank at a level approximating the level of the reaction, gamma-ray dose rates were measured at D's and R's positions and at the film badge rack. Measurements were made with 0.025-r ionization chambers and gamma rate meters, and agreement between the two methods was quite good. The results of these measurements are shown in Table XXX. Calibration of the Co^{60} source gave a dose rate of 4.4 r/min at a rate of 1 ft, which is in good agreement with the rated source strength of 20 curies.

Using a transmission factor of 7×10^{-6} and a reading of 670 mr at the film badge rack, extrapolation to a position 1 ft from a point source gave a dose rate of 4.4 r/min at a rate tank gave a total gamma dose of 9.57×10^{4} rads. Similar extrapolations from D's and R's stations could not be made, since their film badges showed readings of 118 and 31.5 r, respectively, most of which was from fission gamma exposure accumulated during subsequent trips near the source. That this was the case is indicated by the gamma-ray transmission factors at their respective stations. These data indicate that D's prompt gamma dose was

approximately 3 times that measured at the film badge rack (or about 2 r), and R's dose was about 2.3 times the dose at the rack (or approximately 1.5 r).

Extrapolation of the total gamma dose at 1 ft from a point source at the center of the fission excursion (assuming no moderator effect) to the dose incident to K's head and xiphoid regions gives a value of ~10,000 r to the head and a slightly higher value to the upper abdominal area. Considering the nature of the data and the extrapolations involved, this is considered to be in reasonable agreement with the values of 7,800 and 9,000 rads derived from the incident neutron dose which were estimated from the P^{32} measurements, and a gamma-to-neutron dose ratio of 3 to 1. The source was not actually a point source, and certainly some of the gamma exposure to the film badges might have been from gamma-ray production in areas away from the immediate source. It is possible also that the observed gamma-ray transmission factors, which varied greatly from point to point because of intervening equipment, etc., were low compared to what actually was the case.

Another estimate of gamma-ray dose may be made strictly on theoretical grounds. Considering fission gamma rays only, the total prompt gamma energy release is variously quoted as from 7.5 to 12 mev per fission. Using 7.5 mev and 1.5×10^{17} fissions, the total gamma energy available is about 1.5×10^{12} ergs. At 100 cm, the energy flux would be 1.5×10^{7} ergs/cm^2. For gamma rays of intermediate energy, an energy flux of 3,000 ergs/cm^2 results in a dose of 1 rad. Therefore, the total fission gamma dose in the region of K's head would be around 4,500 rads and in the region of his xiphoid greater than 6,000 rads. These estimates agree within a factor of 2 with the 3 to 1 ratio of gamma-to-neutron dose, and in view of the complications this is perhaps as good as can be expected.

Table XXXI—Summary of Estimates of K's Radiation Exposure

Region and Conditions	Fast Neutron Dose (rads)	Gamma Dose (rads)	Total Dose (rads)
Head (incident)	2,600	7,800	10,400
Upper abdomen (incident)	3,000	9,000	12,000
Total body (average)	900	3,000-4,000	3,900-4,900

Total Dose (Case K)

As stated previously, both the fast neutron and the gamma-ray doses to K were completely anisotropic. It is possible, therefore, only to estimate his average total-body dose and total incident dose to the head and upper abdominal regions. In many respects, the neutron dose estimates were more satisfactory than those of gamma dose. The most reliable estimates of incident gamma dose to the head and upper abdominal areas, where the effects of the water moderator were minimum, are perhaps those based on a fast neutron-to-gamma dose ratio of 3. Taking the various factors into consideration, what seems to be the most reasonable estimates of K's radiation exposure are summarized in Table XXXI.

The RBE of fission neutrons for the production of lethality in the mouse is approximately 2.[51] The mouse, however, is thin compared to the neutron mean free path, and the neutron dose may be assumed to be isotropic throughout and over the entire body. Since these were not the conditions of K's exposure, it is virtually impossible to choose an appropriate RBE value for the fast neutron component of his dose. Thus, no attempt is made to estimate average total-body exposure in rems. It seems advisable to say only that his average total-body exposure was probably between 3,900 and 4,900 rads, of which about 900 rads was due to fission neutrons, and that a considerably greater portion of the dose was delivered to the upper half of the body than to the lower half.

SECTION VII

Health Physics Studies and Area Radiation Levels

James N. P. Lawrence, M.A.
With the collaboration of Jerome E. Dummer, M.S., Dean D. Meyer, B.S., Leo G. Chelius, M.S., Edwin A. Bemis, Jr., B.A., and others

THE COMPLEX of buildings at the Los Alamos Scientific Laboratory known as DP West is an area in which the principal health hazard is alpha radiation. In these buildings there are some other radiologic hazards, but the greater part of the work in the area involves plutonium. An outline of the principal structures is shown in Fig. 9. The accident occurred in Room 218 of Building 2, and the layout of this room is shown in detail in Fig. 2.

Whenever plutonium in kilogram quantities exists, the possibility of a critical excursion can never be zero. In this instance it was the considered opinion of supervision and also of the Laboratory's Criticality Safety Committee that adequate safeguards for all processes existed, that a critical mass of plutonium could not exist in any one place. For this reason the monitoring personnel assigned to the building were primarily concerned with incidents or accidents involving alpha contamination.

Detection of the Accident

The first indication of the accident outside its immediate vicinity was the activation of a criticality alarm in the north wing of Building 3, the only such alarm in the area. Additional alarms were on order but had not yet been installed. The workers in Building 3 could find no sign of trouble and assumed that the alarm had gone off accidentally for some unknown reason.

At Los Alamos there are eight continuous-recording gamma monitors about the community. Three of these instruments recorded the excursion. In each case the detector was in an unusually favorable position for observing the burst as compared to the other five. Distances from the accident were 3,250, 7,700, and 12,900 ft. Although some of the other stations were closer to the burst, they were well shielded by the terrain from the low-level radiation which was recorded.

The burst was also recorded on the background monitor located on the top of Omega West reactor, about 3,900 ft away in a deep canyon. A sensitive ion chamber for tritium monitoring located in Building 3 of DP West recorded the gamma radiation of the burst, as did a multiple-channel tritium monitor in the same area. All the recorders gave good evidence that only a single burst occurred.

The burst was also indicated on several non-recording instruments. Unusual activity in the alpha hand counters in the area was noted at about the time of the excursion. The activation of the criticality alarm in Building 3 was mentioned above. Approximately five minutes elapsed before this was reported to the area monitoring supervisor. He realized the significance of the report, and this realization subsequently disclosed the site and nature of the accident.

As proof that no significant radiation was received at residential areas, film badges which had been planted on Dec. 22, 1958, were developed on Jan. 5, 1959, and indicated no exposure. The minimum gamma exposure detectable by film badge is about 0.04 r. These films were located at 2,000, 4,700, 7,700, and 12,900 ft from the accident site.

Monitoring and Dosimetry of Personnel

Although film badges capable of recording exposures in the range of 1,000 r were routinely issued to nearly all employees involved in plutonium or uranium operations in this area, the wearing of these devices at all times was not required. Normally the only penetrating radiations to be expected were gamma radiations from fission products contaminating U^{235}, high-energy gamma from contaminants of U^{233}, and low energy x-rays from plutonium. When significant exposure to these radiations was not anticipated, individuals frequently did not remove their film badges from the storage rack,

which was located about 137 ft from the position of the excursion.

The practice of planting film badges in the buildings was not in general use. Films were planted only in vaults where appreciable quantities of fissionable material were stored.

Since a large number of persons involved in the initial appraisal of the accident were not wearing film badges, it was necessary to estimate their exposures. At the same time it was decided to estimate the exposure of everyone employed in the immediate area. A check was made of all persons having access to the site to determine their presence or absence at the time. All craft workers were found to have left the area by 4:30 p.m. on the day of the accident.

A personal interview was held with each individual who normally worked in the area, and with those persons who held badges which would permit their access to the area. In this interview it was determined if and when the person was wearing a film badge and what type of work had been done the previous week while the film badge was worn. Further, an account of the movements of these persons was obtained from 4:30 p.m. to 5:00 p.m. on the day of the accident.

At 6:00 p.m. most of the film badges issued to DP West personnel were collected and processed. This included 46 film badges which were not worn at the time of the accident but were located in the storage rack 137 ft from the burst. The highest readings were from the badges of D and R, who assisted K from the room following the nuclear excursion. Unfortunately, K was not wearing his film badge at the time of the accident. The average exposures and standard deviations of the exposures to the 46 films in the film badge rack were: 0.67 ± 0.09 r gamma; 0.23 ± 0.04 rem thermal neutrons; and 1.3 ± 0.21 rem fast neutrons. The fast neutron exposure was determined with Kodak's Personal Monitoring Film Type 2B, as designed by J. S. Cheka of Oak Ridge.[55] The thermal neutron and gamma exposures were evaluated by the method devised by Kalil.[56]

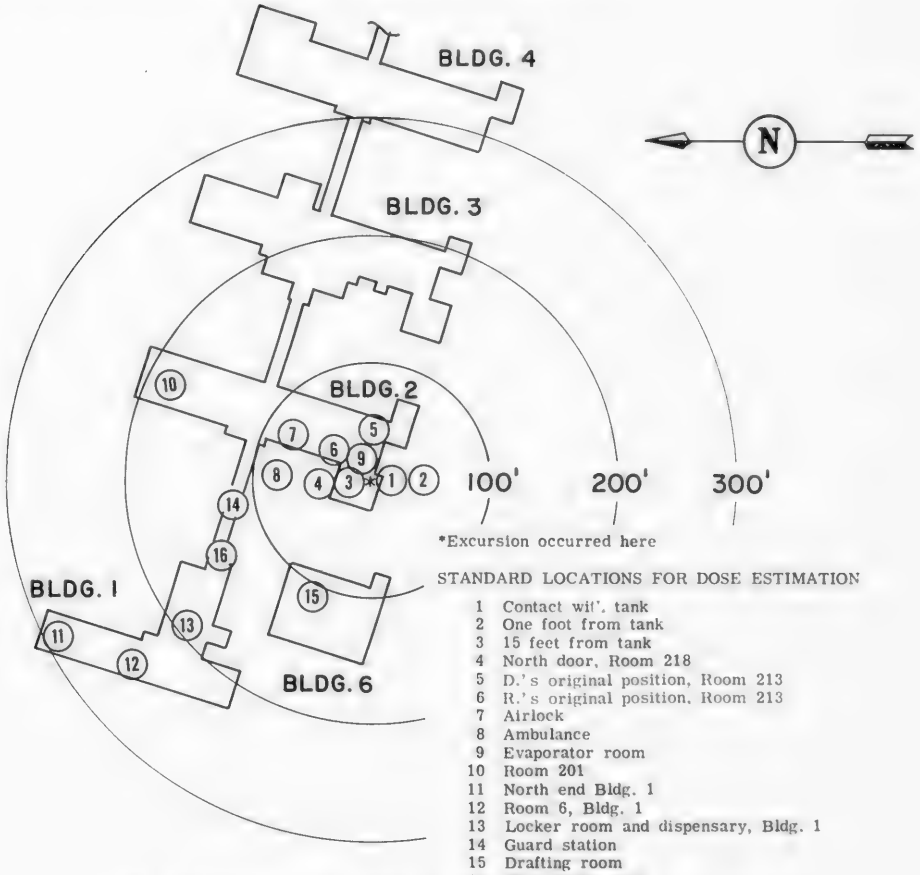


Fig. 9—Structures at DP West showing location of critical excursion.

Numerous field surveys were made with both G-M tube and ionization chamber instruments. Nearly 100 separate dose rate measurements were made and recorded between 4:40 p.m. on Dec. 30, and 3:30 p.m. on Jan. 1. In many cases dose rates measured at the same location did not decrease according to the $t^{-1.2}$ law, probably because of minor differences in location and differences in personal judgment in reading the instruments. For purposes of calculation the expected readings at specific locations of interest were calculated according to $t^{-1.2}$. The average of these values was used for dosage calculation in some instances.

Attenuation factors at a number of different locations were determined several days after the accident (Section VI). From these data, dose rates at various positions were related to the dose at the film badge rack.

No practical experiment was conceivable for determining the neutron attenuation. For all positions closer to the burst than the film badge rack, a simple inverse-square attenuation was assumed. However, nuclear-track films located about 270 ft from the burst indicated an absorption attenuation of 1/5 in addition to the inverse-square decrease. It was assumed, therefore, that the absorption attenuation increased linearly with distance beyond the film badge rack.

For lack of better data, it was assumed that the gamma dose fell inversely as the square of the distance with a similar absorption attenuation factor at 270 ft from the excursion, and that this attenuation increased linearly with distance beyond the film badge rack. There has been no opportunity to verify this assumption other than recognition of the fact that no gamma exposure was indicated on film badges located about 270 ft from the burst.

It was also determined from film badges that the average exposure to personnel in Room 201 of Building 2 was 0.23 r gamma with 0.14 rem fast neutron exposure and no thermal neutron exposure.

The effect of large-diameter sources on meter readings taken near the tank was computed. It was found that for a source 15 in in diameter, a monitoring instrument in contact with the tank (19 in from center of tank) would respond according to inverse-square predictions. For a source the size of the tank, i.e., about 38 in in diameter, the instrument response would be 1.5 times that predicted by simple inverse-square at the surface of the tank, about 1.1 times inverse-square predictions at 9 in from the surface of the tank, and in accordance with inverse-square prediction at 20 in from the tank. For the burst the small-diameter source was assumed, and for the residual gamma, the large source was assumed (due to the mixing action of the stirrer).

Table XXXII—Tabulation for Health Monitor U

Time	Location	Calculated Exposure (r)
4:35 p.m.*	At coverall check station	1.50
4:40 p.m.	Answered R's call for help	
4:41 p.m.	Checked K for alpha in air lock	0.07
4:44 p.m.	Entered Room 218 by north door	
	Assume: First 5½ min in location 3	2.46
	Assume: ½ min in location 2	6.52
4:50 p.m.	Left Room 218 to get gamma survey meter in Room 201	
4:52 p.m.	Arrived to hear "clear area call" and left area	
Total		10.55
Burst fast neutron (rem)		3.08
Burst thermal neutron (rem)		0.54

Film badge worn for entire operation indicated 9.3 r gamma

Total exposure 9.3 + 3.08 + 0.54 = 12.92 rem

*Time of burst.

Table XXXIII—Tabulation for Ten Individuals

Individual	Total Dose (rem)
S	12.46
T	8.18
U	12.92
C	1.09
W	6.83
X	10.12
Y	0.51
Z	10.24
R	53.74
D	133.54

By using the monitoring measurements at several positions close to the tank, integration of a $t^{-1.2}$ function, the total attenuation factor from the tank to the film badge rack determined with Co^{60}, and the effect of the 38-inch-diameter source of gamma, it was determined that 96% of the radiation exposure as recorded at the film badge rack was due to the burst plus one second thereafter, and 4% due to the residual gammas from the fission products. Although this is not the ratio of prompt gamma mev to residual gamma mev over the time period considered, Harris[57] reports that he has also observed that most of the gamma radiation detected by film badges is due to the burst plus one second and not due to the residual gammas.

Had every individual in the general vicinity been wearing a film badge at the time of the critical excursion, the task of recording all

Table XXXIV—Estimated Exposure of Case K, Assuming Three Possible Positions at Time of Burst

Time	Location	Chest at Contact (r)	Back When Chest Was at Contact (r)	Chest at 6 in (r)	Back When Chest Was at 6 in (r)	Chest at 12 in (r)	Back When Chest Was at 12 in (r)
4:35 p.m.	At tank	4×10^{4}	1.9×10^{4}	2.3×10^{4}	1.3×10^{4}	1.5×10^{4}	9.1×10^{3}
4:35 p.m.	Residual, 1 to 20 sec	2.5×10^{2}	1.2×10^{2}	1.4×10^{2}	8.1×10^{1}	9.5×10^{1}	5.7×10^{1}
4:33-35 p.m.	Remainder insignificant with respect to instantaneous exposures						
Total		4.25×10^{4}	2.02×10^{4}	2.44×10^{4}	1.38×10^{4}	1.6×10^{4}	9.67×10^{3}

personnel exposures would have been relatively easy. As has been mentioned above, this unfortunately was not the case. Many hours were spent interviewing a large number of workers and charting their movements on a minute-by-minute basis. In some cases conflicting statements had to be resolved. Eleven individuals were of particular interest even though some of them were some distance from the excursion at the time of the accident. The following listing indicates the positions of these people at 4:35 p.m., the time of the accident:

S, health Monitor	Bldg. 2 mezzanine, 200 ft from excursion
T, health Monitor	Dispensary, Bldg. 1, 160 ft from excursion
U, health Monitor	Check station, Bldg. 2, 95 ft from excursion
C, monitoring Supervisor	Office, Bldg. 1, 240 ft from excursion
W, group Leader	Office, Bldg. 1, 260 ft from excursion
X, chemical Operator	Room 201, Bldg. 2, 180 ft from excursion
Y, nurse	Office, Bldg. 1, 210 ft from excursion
Z, operation Supervisor	Drafting room, Bldg. 6, 100 ft from excursion
R, chemical Operator	Room 213, Bldg. 2, 36 ft from excursion
D, chemical Operator	Room 213, Bldg. 2, 43 ft from excursion
K, chemical Operator	Room 218, Bldg. 2, Beside excursion tank

The movements of these as well as many other people was plotted for each minute of the next 25 minutes. From these findings and from the attenuation studies mentioned previously, a dose was estimated for each individual. Table XXXII shows a typical tabulation for Health Monitor U who, it will be seen, was wearing a film badge. His exposure was also calculated from his movements, however, and the agreement of the two figures for gamma dose is quite acceptable. It will also be noted that neutron doses are listed in rem, as this is the standard method of reporting such exposures for record purposes even though the RBE factor may be open to some question.

Similar calculations were made for all other individuals in the vicinity, and Table XXXIII indicates their estimated doses. Exposures to all other personnel were lower than the ones in this table.

Using the factors previously mentioned, K's gamma dose from the burst and residual gammas was estimated for three possible positions at the time of the burst. In Table XXXIV estimates are given for his chest and back assuming that his chest was in contact with the tank, 6 in from the tank, and 12 in from the tank. It should be pointed out, however, that these calculations were based on the assumption that K was standing on the floor rather than on the stepladder. The latter assumption was used in the calculations in Section VI, which explains the difference in results. The best guess is that he *was* on the stepladder.

SECTION VIII

Report on Other Personnel Exposed

Thomas L. Shipman, M.D.

IN THE CASE of an accident such as the one described in this paper most of the interest is focused on the most heavily irradiated case. As shown in Section VII, however, a number of other individuals received measurable overexposures. Of these, only the two significant exposures will be considered here: Case D, whose dose was approximately 130 rads, and Case R, with a dose of approximately 35 rads. In both of these cases the majority of the exposure was to gamma rays rather than neutrons. In both cases the only significant findings are the alterations in the blood counts, and it is of interest to compare these with the changes observed in the Rongelap natives[58] and in the Oak Ridge cases.[6]

Case D

D, it will be recalled, was at work in the room next to the one in which K was exposed (Fig. 2). D's exposure from the critical excursion itself was negligible, a total of only about 3 rads. He did, however, enter the room of the accident twice, and in these visits he unquestionably passed within a few feet of the highly radioactive tank at least four times. His total dose was approximately 130 rads, neutrons and gamma.

D's blood chemistry has already been discussed in Section III. It may be stated that at no time did he show evidence of any signs or symptoms, objective or subjective, which could not be attributed to his concern for his fellow worker, K. He had no nausea or vomiting, no weakness. He developed no petechiae, no loss of hair, and his only apprehension was for K. Some months later he developed one transient respiratory infection and also underwent a full-mouth extraction of his teeth for an infectious process that antedated the accident.

The changes in his blood picture, however, were both interesting and dramatic (Fig. 10). D's preexposure blood counts were well known. Over a period of approximately 10 years he had had 24 blood counts done, all of them by the same group of technicians, and one of these technicians did all save a few of the postexposure counts.

Leukocytes—D's preexposure white blood cell count averaged 8,300/mm³, with extremes of 10,600 and 6,200. His absolute granulocyte count averaged 4,785, and his average lymphocyte count was 2,650/mm³. The first postexposure count, done about two hours after the accident, showed a rise in total leukocytes and in granulocytes to 10,900 and 7,200, respectively, but a drop in the absolute lymphocyte count to

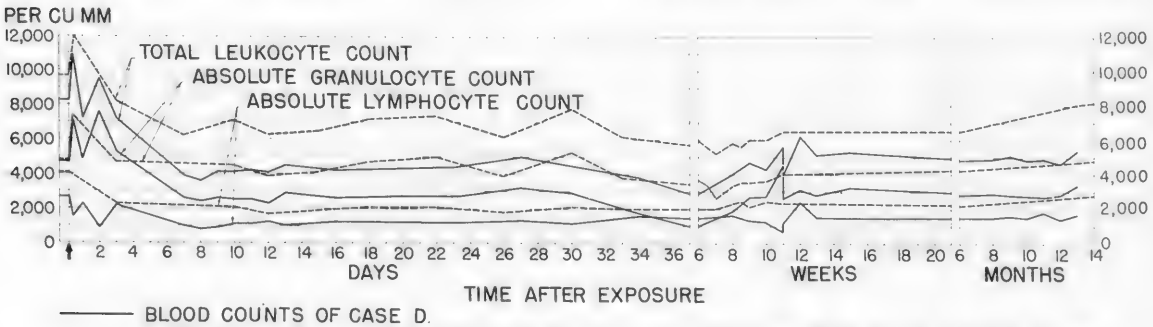

PER CU MM
12,000
10,000
8,000
6,000
4,000
2,000
0
TOTAL LEUKOCYTE COUNT
ABSOLUTE GRANULOCYTE COUNT
ABSOLUTE LYMPHOCYTE COUNT
1 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 6 8 10 12 14 16 18 20 6 8 10 12 14
DAYS
WEEKS
MONTHS
TIME AFTER EXPOSURE
BLOOD COUNTS OF CASE D.
AVERAGE BLOOD COUNTS OF RONGELAP NATIVES. (THE FIRST-DAY PEAK IN THE COUNTS OF THE MARSHALL ISLANDERS IS ASSUMED AND WAS NOT OBSERVED. THEIR FIRST COUNTS WERE DONE ON THE THIRD DAY.)

Fig. 10—Blood changes in Case D compared with those of the Rongelap natives.

1,463. During the next 48 hours the leukocyte and granulocyte counts fluctuated rather widely, the lymphocyte count showing a moderate fluctuation. On the morning of the third day after the accident, the total white cell count was 7,200, and the absolute granulocyte and lymphocyte counts were 5,328 and 1,224 respectively. All counts dropped progressively until the eighth day, at which time a low point seemed to be reached. On this day the total WBC was 3,600 and the granulocytes and lymphocytes fell to 2,484 and 864. This drop was followed by a slight rise, followed by a leveling off until about the end of the fourth week when the total white cell count and the granulocyte count seemed to drop again.

The blood counts taken on the 34th and 37th days were done at a laboratory in another state. It would appear, however, from a comparison with the cases of the Rongelap natives,[58] as well as other accident cases,[1, 2, 4, 5] that this drop at around the fifth week is to be expected, although the reason for this is not yet clear.

During the 11th week D had a mild influenza-like infection, with both respiratory and gastrointestinal symptoms. This cleared up without any treatment other than rest at home. From that time on there was surprisingly little change in the counts of any of the white cells through the 13th month. The final counts at the time of writing showed a total WBC of 5,400, a granulocyte count (absolute) of 3,402 and a lymphocyte count of 1,674. These final counts, however, all show an increase above the previous month, and it may be that recovery in the next year will be more pronounced.

Abnormal Cells—During the first five months after the accident, atypical lymphocytes were seen in almost every smear in percentages varying from 1 to 6. One binucleated lymphocyte was seen in the third month. There did not, however, seem to be any significant pattern in the occurrence of these cells. There was no significant or consistent shift in the ratio of segmented and band-type granulocytes.

Erythrocytes—The preexposure average number of red cells was 5.38 million, with an average hemoglobin level of 16.9 gm. Both showed a tendency to drop somewhat in the first two months, although this drop was neither dramatic nor consistent. The lowest levels noted in this period were 4.77 million and 15.3 gm. The average red cell count in the 13 months following the accident was 5.03 million, and the average hemoglobin level, 15.9 gm. No reticulocytes had been noted in any preaccident smears but some were seen in almost all subsequent smears through the third month. The largest number noted in any smear was 2.6%.

Table XXXV—Average Blood Levels for R

	Eight Years Preaccident	Thirteen Months Postaccident
RBC	5.19 million	5.15 million
Hgb	16.2 gm	16.4 gm
WBC	6,471	5,300
Granulocytes (absolute)	3,980	3,240
Lymphocytes (absolute)	1,870	1,570

Platelets—The number of platelets seemed to show a slight fall until about the 10th week, after which there was a return to normal. It is questionable whether this drop was of statistical significance, and it certainly would not be proper to compare our findings with those of other laboratories using other methods of counting platelets or even other technicians using the same method. In this one case, however, it appears that alterations in the platelet count were of no clinical significance.

Had it not been for previous experience with cases of radiation exposure in the same general dose range, D's alteration in blood counts would have been rather alarming. He followed, however, much the same course as previous cases, and his general state of well-being was entirely unimpaired. At the time of the accident he was 37 years old, tall, lean, and in unusually good physical condition. He was proud of his muscular vigor and firmly denied any sign of weakness or any other symptom, either subjective or objective.

Case R

As has been described, R received a total dose of approximately 35 rads, principally gamma radiation received when he entered the room in which the accident occurred in order to assist K. He passed twice within a few feet of the tank in which the reaction took place. His dose is quite compatible with these actions.

Studies on R were confined largely to those indicated from a clinical point of view. His blood findings are shown in Table XXXV, where it will be noted that his erythrocyte count dropped less than 1% on the average, while his average hemoglobin level actually increased about 1%. These changes are regarded as of no statistical significance.

The decrease in total leukocyte count, granulocyte count, and lymphocyte count are obviously of some significance, although his most recent counts are well within his preaccident range. Like D, R at no time showed any unusual signs or symptoms and he lost no time away from his work.

Discussion

The records for each of these men present food for speculation. On the chart showing the blood levels of D, there are also shown the average blood levels of the Rongelap natives over a similar period (Fig. 10). The native controls had levels slightly higher than D to start with and the Rongelap counts did not go as low as his, although their radiation doses were slightly higher, 175 rads as compared to 130 rads. But after more than a year neither the levels of the natives nor those of D had returned to their previous norms.

D received his exposure within a few minutes, while the Rongelap doses were spread out over a period of about 48 hours. It is quite possible that we have here an indication of dose rate dependence, although it would be hard to prove this statistically. Furthermore, the Rongelap natives undoubtedly had among them a number of people with chronic and acute infections which possibly had the effect of stimulating leukocyte formation. There is the suggestion in the case of D that all his white cell levels were slightly higher after his respiratory infection in the third month. His levels might have been higher yet had he had a number of mild infections.

The total white blood cell count is of little or no significance in the first 48 hours after exposure to radiation. The absolute lymphocyte count, on the other hand, falls promptly and steadily. Its rate and depth of fall may be used as of some prognostic significance. After 48 hours all leukocytes become fewer, reaching a low point in eight or nine days. After a period of apparent improvement they will again decrease at about the end of the fifth week. Complete return to normal, however, will be extremely slow.

The case of D, together with those of the Rongelap natives, indicates quite conclusively that individuals exposed in the 100- to 200-rad range will in all probability show little or nothing in the way of subjective symptoms. Impressionable patients may become nauseated and complain of weakness, but this is certainly not the rule.

R also presents some interesting points. It is possible to demonstrate a decrease in his leukocyte counts, but only because there existed a firm base line of previous counts. Prior to the accident his highest recorded white count was 9,000, his lowest 4,900. After the accident his highest was 7,200, his lowest 4,100. But without previous counts for comparison with a series of postexposure counts, it seems obvious that such routine hematology is of little diagnostic or prognostic value for exposures in this general range. More research in this area is naturally indicated, but at the present time routine blood studies contribute little to the clinical evaluation of exposures below 50 rads except to provide reassurance that the dose was not far larger than estimated.

On the night of the accident, both D and R were permitted to go home, although both were requested to report to the hospital for observation the following morning. There seemed to be no medical reason for hospitalizing them, and it was felt very strongly that such a course was important for the morale of the men and their families.

SECTION IX

Summary

Thomas L. Shipman, M.D.

THE PRECEDING discussions have presented in considerable detail the various facets of a nuclear criticality accident which resulted in the death of one man and substantial exposures to two others.

The critical excursion took place in a tank of solution from which plutonium was being recovered, and the number of fissions was calculated to be $\sim 1.5 \times 10^{17}$. The average whole body dose to K has been estimated to be between 3,900 and 4,900 rads, with the incident dose to the upper abdomen calculated to be approximately 12,000 rads, neutrons plus gamma. Two other workers received total doses of approximately 130 and 35 rads, respectively, most of this being gamma radiation.

K went promptly into shock and was unconscious within a few minutes of the accident. Neither of the other men showed any signs or symptoms of injury other than alterations in their blood counts. By heroic medical treatment it was possible to get K out of his state of shock, but he died 35 hours after the accident. His clinical course and treatment are described in detail. The most dramatic clinicopathological changes were observed in the hemopoietic and urinary systems. Lymphocytes were not found in the circulating blood after the eighth hour, and there was virtually complete urinary shutdown despite administration of large amounts of fluids.

The gross and microscopic pathology are discussed in Section IV. The changes in the heart and in the gastrointestinal tract were pronounced, as were the changes in the bone marrow.

Section V describes a number of special studies which were carried out, and one of the most significant of these relates to the distribution of plutonium in the man's body. He had worked with plutonium for a number of years, although he had never had a significant overexposure. A surprisingly large percentage of the material was recovered from the pulmonary lymph nodes.

Sections VI and VII are concerned with the dosimetry of the fatal case and give in detail the various studies which were carried out to establish the dose levels of other workers less seriously involved. In the case of K it is clearly apparent that the dose varied widely in different parts of the body and even in different parts of the same organ, such as the heart or the stomach.

Cases D and R received doses of approximately 130 and 35 rads, respectively. The changes in their blood counts are given in Section VIII. It appears that the changes following exposures in excess of 100 rads are characteristic and of clinical significance, whereas doses below 50 rads produce blood changes which are too slight to be of any diagnostic value.

References

1. Hempelmann, L. H.; Lisco, H.; and Hoffman, J. G.: *Ann. Int. Med.* 36: No. 2:279-510, 1952.
2. Jammet, H., et al.: *Rev. franc. d'etudes clin. et biol.* 4:210, 1959.
3. Mathe, G., et al.: *Rev. franc. d'etudes clin. et biol.* 4:226, 1959.
4. Hasterlik, R. J., and Marinelli, L. D.: Proc. Internat. Conference on the Peaceful Uses of Atomic Energy 11:25, 1956.
5. Guskova, A. K., and Baisosolov, G. D.: Proc. Internat. Conference on the Peaceful Uses of Atomic Energy 11:35, 1956.
6. Brucer, M., et al.: The Acute Radiation Syndrome, Oak Ridge Institute of Nuclear Studies Report ORINS-25, 1959.
7. Paxton, H. C., et al.: Los Alamos Scientific Laboratory Report LAMS-2293, 1959.
8. Paxton, H. C., et al.: *Nucleonics* 17, No. 4:107 1959.
9. Langham, W. H., et al.: *Rad. Res.* 5:404, 1959.
10. Petersen, D. F.; Lushbaugh, C. C.; and Lee, P.: *Fed. Proc.* 16:327, 1957.
11. Petersen, D. F., and Hughes, L. B.: *Rad. Res.* 9:166, 1958.
12. Karmen, A.: *J. Clin. Invest.* 34:131, 1955.
13. Wróblewski, F., and LaDue, J. S.: *Proc. Soc. Exper. Biol. & Med.* 91:569, 1956.
14. Hill, B. S., and Levi, C.: *Cancer Res.* 14:513, 1954.
15. Siegel, A., and Bing, R. J.: *Proc. Soc. Exper. Biol. & Med.* 91:604, 1956.
16. Dunn, M.; Martins, J.; and Reismann, K. R.: *J. Lab. & Clin. Med.* 51:259, 1958.

17. Lushbaugh, C. C.; Hughes, L. B.; and Hale, D. B.: *Fed. Proc.* 15:523, 1956.
18. Winkler, C., and Paschke, G.: *Rad. Res.* 5:156, 1956.
19. Kyker, G. C.: The Acute Radiation Syndrome, Oak Ridge Institute of Nuclear Studies Report ORINS-25, p. 7.1, April 1959.
20. Dacie, J. V.: *Nature* 166:36, 1950.
21. Goodall, McC., Stone, C., and Hayes, B. W., Jr.: *Ann. Surg.* 145:479, 1957.
22. Kretchmar, A. L.: Personal communication, 1959.
23. Kay, R. E.; Early, J. C.; and Entenman, C.: *Rad. Res.* 6:98, 1957.
24. Rubini, J. R.: The Acute Radiation Syndrome, Oak Ridge Institute of Nuclear Studies Report ORINS-25, p. 6.1, April 1959.
25. Rubni, J. R.; Cronkite, E. P.; Bond, V. P.; and Fliedner, T. M.: *Proc. Soc. Exper. Biol. & Med.* 100:130, 1959.
26. Dische, Z.: *J. Biol. Chem.* 181:379, 1949.
27. Parijek, J.; Arient, M.; Dienstbier, Z.; and Skoda, J.: *Nature,* London 182-721, 1958.
28. Petersen, D. F.; Murray, A., III; and Magee, M.: Unpublished data.
29. Williams, C. M.; Krise, G. M.; Anderson, D. R.; and Dowben, R. M.: *Rad. Res.* 7:176, 1957.
30. Taussky, H. H.: *Clin. et chim. acta* 1:224, 1956.
31. Goldbarg, J. A., and Rutenburg, A. M.: *Cancer* 11:283, 1958.
32. Pickering, J. E., et al.: Los Alamos Scientific Laboratory Report LA-1910 (Del.), 1956.
33. Hurst, G. S.: Private communications to W. H. Langham, Dec. 31, 1958, and Jan. 2, 1959.
34. Richmond, C. R.: Los Alamos Scientific Laboratory Report LA-2207, 1958.
35. Hevesy, G.: Radioactive Indicators, New York, Interscience Publishers, Inc., 1948, p. 207.
36. Davies, R. E.; Kornberg, H. L.; and Wilson, G. M.: *Biochem. J.* 52; Comm. XV, 1952.
37. International Commission on Radiological Proctection Report (Committee II), to be published.
38. Spector, W. S.: Handbook of Biological Data, Philadelphia, W. B. Saunders Co., 1956.
39. Edelman, I. S.; James, A. H.; and Moore, F. D.: Metabolic Interactions, New York, Josiah Macy, Jr. Foundation, 1952, p. 240.
40. Berenblum, I., and Chain, E.: *Biochem. J.* 32:295, 1938; see modification by Weil-Malherbe, H.: *Biochem. J.* 49:286, 1951.
41. Fiske, C. H., and Subbarrow, Y.: *J. Biol. Chem.* 66:375, 1926.
42. Perley, A.; Langham, W. H.; and Hoffman, J. G.: Los Alamos Scientific Laboratory, unpublished data, 1946.
43. Evans, R. J., and St. Johns, J. L.: *Indust. & Engin. Chem. (Anal. Edit.)* 16:630, 1944.
44. Schwendiman, L. C.; Healy, J. W.; and Reid, D. L.: Hanford Atomic Products Operation Report HW-22680, 1951.
45. Langham, W. H.: *Brit. J. Radiol.,* Suppl. 7:95-113, 1957.
46. Lawrence, J. N. P.: Los Alamos Scientific Laboratory Report LA-2329, 1959.
47. National Bureau of Standards Handbook No. 69, Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water, Washington 25, D.C., U. S. Govt. Printing Office, 1959.
48. Langham, W. H.: *Health Physics* 2:172, 1959.
49. Carritt, J.; Fryxell, R.; Kleinschmidt, J.; Kleinschmidt, R.; Langham, W. H.; San Pietro, A.; Schaffer, R.; and Schnap, B.: *J. Biol. Chem.* 171:273, 1947.
50. Recommendations of the International Commission on Radiological Protection, *Brit. J. Radiol.* Supp. 6, 1954.
51. Accidental Radiation Excursion at the Y-12 Plant, June 16, 1958. U. S. Atomic Energy Commission Report Y-1234, July 28, 1958, Office of Technical Services, U. S. Dept. of Commerce, Washington 25, D.C.
52. Price, B. T.; Horton, C. C.; and Spinney, K. T.: Radiation Shielding, International Series of Monographs on Nuclear Energy, Division 10, Reactor Design Physics, New York, Pergamon Press, 1957, Vol. 2, p. 287.
53. Price, B. T.; Horton, C. C.; and Spinney, K. T.[52] Vol. 2, p. 178.
54. Storer, J. B.; Harris, P. S.; Furchner, J. E.; and Langham, W. H.: The Relative Biological Effectiveness of Various Ionizing Radiations in Mammalian Systems, *Rad. Res.* 6:188-288, 1957.
55. Cheka, J. S.: *Nucleonics* 12:40 (No. 6) 1954.
56. Kalil, F.: Los Alamos Scientific Laboratory Report LA-1923. April 1955.
57. Harris, P. S.: Personal communication, 1959.
58. Cronkite, E. P.; Bond, V. P.; and Dunham, C. L.: Some Effects of Ionizing Radiation on Human Beings, U. S. Atomic Energy Commission Report TID-5358, 1956.